

Devi, S.
09/613092

09/613092

~~FILE~~ ~~URGENT~~ ENTERED AT 12:32:26 ON 15 AUG 2002
L1 10 SEA ABB=ON PLU=ON TVSRVPWTAWAFHGY|RSYQHDLRAYGFWRL|LVRRF
VHRRPHVESQ/SQSP

Seq. 1Ds
5-7

~~FILE~~ ~~URGENT~~ ENTERED AT 12:33:56 ON 15 AUG 2002
L2 4 SEA ABB=ON PLU=ON L1

L2 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:199850 HCAPLUS

TITLE: Inhibition of pneumococcal carriage in mice by
subcutaneous immunization with peptides from the
common surface protein pneumococcal surface
adhesin A

AUTHOR(S): Johnson, Scott E.; Dykes, Janet K.; Jue, Danny
L.; Sampson, Jaquelyn S.; Carlone, George M.;
Ades, Edwin W.

CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases,
National Center for Infectious Diseases, Centers
for Disease Control and Prevention, Atlanta, GA,
30333, USA

SOURCE: Journal of Infectious Diseases (2002), 185(4),
489-496

CODEN: JIDIAQ; ISSN: 0022-1899

PUBLISHER: University of Chicago Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pneumococcal surface adhesin A (PsaA), a common protein expressed on
all 90 pneumococcal serotypes, is a vaccine candidate. Three
anti-PsaA monoclonal antibody phage display-expressed mono-peptides
(15 mers), in various formulations as lipidated or nonlipidated
multiantigenic peptides or as bi- or tripeptide constructs, were
studied in a mouse nasopharyngeal carriage model to det. the
inhibitory effect of induced antibodies on carriage of pneumococcal
serotypes 2, 4, and 6B. Antibodies to each of the various peptides
tested reduced carriage of the 3 serotypes. Redn. in carriage by
nonlipidated multiantigenic peptide antibodies was highly variable
(39%-94%; mean, 59%; std. deviation [SD], 20.2%); however,
more-consistent results were obsd. in mice immunized with lipidated
(56%-98%; mean, 69%; SD, 13.6%) and combination or bi-peptide
(55%-91%; mean, 76%; SD, 13.1%) formulations. These peptides are
immunogenic, and their induced antibodies reduce carriage in mice.
PsaA peptides demonstrate potential for being important new vaccines
against pneumococcal carriage, otitis media, and invasive
pneumococcal disease.

IT 241814-51-7 241814-52-8 241814-53-9

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of pneumococcal carriage in mice by s.c. immunization
with peptides from common surface protein pneumococcal surface
adhesin A)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L2 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:51509 HCAPLUS

DOCUMENT NUMBER: 136:117369

TITLE: Multiple antigenic peptides induce protective
immune response against Streptococcus pneumoniae

Searcher : Shears 308-4994

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INVENTOR(S): Ades, Edwin W.; Johnson, Scott E.; Jue, Danny
L.; Sampson, Jacquelyn S.; Carlone, George M.
PATENT ASSIGNEE(S): The Government of the United States of America,
as Represented by the Secretary, Department of
Health and Human Services, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004497	A2	20020117	WO 2001-US21626	20010710
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2000-613092 A2 20000710

AB The authors disclose the cloning and immunogenicity of the pneumococcal surface A protein (PspA) of *S. pneumoniae* challenge. In addn., the authors disclose epitope mapping for anti-PspA monoclonal antibodies obtained by panning of a phage display library. In one example, immunization of xid mice with PspA provided protective immunity against subsequent challenge. A in a second example, immunization of Balb/C mice with lipidated peptides or multiple antigenic peptide constructs were shown to inhibit bacterial colonization.

IT **241814-51-7D**, TVSRVPWTAWAFHGY, multiple antigenic peptide conjugates **241814-52-8D**, RSYQHDLRAYGFWRL, multiple antigenic peptide conjugates **241814-53-9D**, LVRRFVHRRPHVESQ, multiple antigenic peptide conjugates **390747-42-9 390747-44-1 390747-45-2 390747-46-3 390747-48-5 390747-49-6**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective immune response against *Streptococcus pneumoniae* is induced by)

L2 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:273192 HCAPLUS

DOCUMENT NUMBER: 133:295042

TITLE: Selection of an immunogenic and protective epitope of the PsaA protein of *Streptococcus pneumoniae* using a phage display library

AUTHOR(S): Srivastava, N.; Zeiler, J. L.; Smithson, S. L.; Carlone, G. M.; Ades, E. W.; Sampson, J. S.; Johnson, S. E.; Kieber-Emmons, T.; Westerink, M. A. J.

Searcher : Shears 308-4994

09/613092

CORPORATE SOURCE: Department of Medicine, Medical College of Ohio,
Toledo, OH, 43614, USA
SOURCE: Hybridoma (2000), 19(1), 23-31
CODEN: HYBRDY; ISSN: 0272-457X
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Streptococcus pneumoniae is an important pathogen that causes disease in young and elderly individuals. The currently available polysaccharide vaccines have limited efficacy in those age groups most susceptible to pneumococcal infections. This study focuses on mapping the epitopes of a surface protein of S. pneumoniae by biopanning a 15 mer phage display library using 5 different monoclonal antibodies (MAbs) against the Pneumoccal surface adhesin A (PsaA). PsaA is a component of the bacterial cell wall that is highly species specific and is involved in bacterial adherence and virulence. Biopanning of the phage display library reveals three distinct epitopes on the PsaA protein. The sequence homol. of these epitopes ranges from two to six amino acids when compared to the native PsaA protein type 2. Two of these epitopes have been evaluated for their immunogenicity in mice. The peptide selected by the MAbs 8G12, 6F6, and 1B7 is referred to as the consensus peptide and is immunogenic in mice. Optimal anti-PsaA response is obsd. in mice immunized with 50 .mu.g of the consensus peptide complexed to proteosomes in 1:1 ratio. The anti-PsaA response is significantly lower than the response to the PsaA native protein. The peptide selected by monoclonal antibody 4E9 in its lipidated form is significantly protective in mice challenged with S. pneumoniae serotype 2 when compared to mice immunized with the native protein. These results show that the selected epitopes of PsaA protein are immunogenic and protective in mice. These epitopes need to be evaluated further as alternatives to currently available vaccines.

IT 301300-55-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PsaA protein of Streptococcus pneumoniae in vaccine against streptococcal infections)

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:577027 HCAPLUS

DOCUMENT NUMBER: 131:198616

TITLE: Epitope peptides immunogenic against Streptococcus pneumoniae and their use in vaccines

INVENTOR(S): Carlone, George M.; Ades, Edwin W.; Sampson, Jacquelyn S.; Tharpe, Jean A.; Zeiler, Joan Louise; Westerink, Maria Anna Julia

PATENT ASSIGNEE(S): The Government of the United States of America, Represented by the Secretary, USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

Searcher : Shears 308-4994

09/613092

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945121	A1	19990910	WO 1999-US4326	19990226
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2326408	AA	19990910	CA 1999-2326408	19990226
AU 9927950	A1	19990920	AU 1999-27950	19990226
BR 9908476	A	20001205	BR 1999-8476	19990226
EP 1060249	A1	20001220	EP 1999-908543	19990226
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

PRIORITY APPLN. INFO.:

US 1998-76565P P 19980302
WO 1999-US4326 W 19990226

AB Peptides are provided which immunospecifically bind to monoclonal antibodies specific for the 37-kDa pneumococcal surface adhesion A protein (PsaA) of Streptococcus pneumoniae of the invention, and that are immunogenic against Streptococcus pneumoniae infection. Also provided are vaccines comprising such immunogenic polypeptides, and methods of conferring protective immunity against Streptococcus pneumoniae infection by administering therapeutic compns. comprising the immunogenic peptides of the invention. Also provided are methods of detecting the presence of Streptococcus pneumoniae in a sample using antibodies or antigens, and methods of preventing and treating Streptococcus pneumoniae infection in a subject. In addn. a phage display method of identifying the sequence of a peptide potentially capable of eliciting protective immunity against a pathogenic microorganism is provided.

IT 241814-51-7P 241814-52-8P 241814-53-9P

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(epitope peptides immunogenic against Streptococcus pneumoniae and their use in vaccines)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

~~FILE 'REGISTRY'~~ ENTERED AT 12:35:08 ON 15 AUG 2002

L3 10 SEA FILE=REGISTRY ABB=ON PLU=ON (241814-51-7/BI OR 241814-52-8/BI OR 241814-53-9/BI OR 301300-55-0/BI OR 390747-42-9/BI OR 390747-44-1/BI OR 390747-45-2/BI OR 390747-46-3/BI OR 390747-48-5/BI OR 390747-49-6/BI)

L4 10 L3 AND L1

L4 ANSWER 1 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 390747-49-6 REGISTRY

CN L-Norleucine, L-threonyl-L-valyl-L-seryl-L-arginyl-L-valyl-L-prolyl-L-tryptophyl-L-threonyl-L-alanyl-L-tryptophyl-L-alanyl-L-

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phenylalanyl-L-histidylglycyl-L-tyrosyl-N6-[L-seryl-L-tyrosyl-L-glutaminyl-L-histidyl-L-.alpha.-aspartyl-L-leucyl-L-arginyl-L-alanyl-L-tyrosylglycyl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-leucyl-N6-(L-leucyl-L-valyl-L-arginyl-L-arginyl-L-phenylalanyl-L-valyl-L-histidyl-L-arginyl-L-prolyl-L-histidyl-L-valyl-L-.alpha.-glutamyl-L-seryl-L-glutaminyl)-L-lysyl-L-norleucyl]-L-lysyl- (9CI) (CA INDEX NAME)

CI MAN

SQL 47,17,16,14

SEQ 1 TVSRVPWTAW AFHGYKX

=====

HITS AT: 1-15

SEQ 1 SYQHDLRAYG FWRLKX

SEQ 1 LVRRFVHRPH VESQ

REFERENCE 1: 136:117369

L4 ANSWER 2 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 390747-48-5 REGISTRY

CN L-Norleucine, N-(1-oxohexadecyl)-L-cysteinyl-L-seryl-L-seryl-L-threonyl-L-valyl-L-seryl-L-arginyl-L-valyl-L-prolyl-L-tryptophyl-L-threonyl-L-alanyl-L-tryptophyl-L-alanyl-L-phenylalanyl-L-histidylglycyl-L-tyrosyl-N6-[N-(1-oxohexadecyl)-L-cysteinyl-L-seryl-L-seryl-L-seryl-L-tyrosyl-L-glutaminyl-L-histidyl-L-.alpha.-aspartyl-L-leucyl-L-arginyl-L-alanyl-L-tyrosylglycyl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-leucyl-N6-[N-(1-oxohexadecyl)-L-cysteinyl-L-seryl-L-seryl-L-leucyl-L-valyl-L-arginyl-L-arginyl-L-phenylalanyl-L-valyl-L-histidyl-L-arginyl-L-prolyl-L-histidyl-L-valyl-L-.alpha.-glutamyl-L-seryl-L-glutaminyl]-L-lysyl-L-norleucyl]-L-lysyl- (9CI) (CA INDEX NAME)

CI MAN

SQL 56,20,19,17

SEQ 1 CSSTVSRVPW TAWAFHGYKX

=====

HITS AT: 4-18

SEQ 1 CSSSYQHDLR AYGFWRKX

SEQ 1 CSSLVRRFVH RPHVESQ

REFERENCE 1: 136:117369

L4 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 390747-46-3 REGISTRY

CN L-Norleucine, N2,N6-bis[L-threonyl-L-valyl-L-seryl-L-arginyl-L-valyl-L-prolyl-L-tryptophyl-L-threonyl-L-alanyl-L-tryptophyl-L-alanyl-L-phenylalanyl-L-histidylglycyl-L-tyrosyl-N6-(L-leucyl-L-valyl-L-arginyl-L-arginyl-L-phenylalanyl-L-valyl-L-histidyl-L-arginyl-L-prolyl-L-histidyl-L-valyl-L-.alpha.-glutamyl-L-seryl-L-glutaminyl)-L-lysyl-L-norleucyl]-L-lysyl- (9CI) (CA INDEX NAME)

CI MAN

SQL 64,19,17,14,14

SEQ 1 TVSRVPWTAW AFHGYKXKX

=====

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HITS AT: 1-15

SEQ 1 TVSRVPWTAW AFHGYKX
=====

HITS AT: 1-15

SEQ 1 LVRRFVHRPH VESQ

SEQ 1 LVRRFVHRPH VESQ

REFERENCE 1: 136:117369

L4 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 390747-45-2 REGISTRY

CN L-Norleucine, N2,N6-bis[N-(1-oxohexadecyl)-L-cysteinyl-L-seryl-L-seryl-L-threonyl-L-valyl-L-seryl-L-arginyl-L-valyl-L-prolyl-L-tryptophyl-L-threonyl-L-alanyl-L-tryptophyl-L-alanyl-L-phenylalanyl-L-histidylglycyl-L-tyrosyl-N6-[N-(1-oxohexadecyl)-L-cysteinyl-L-seryl-L-seryl-L-leucyl-L-valyl-L-arginyl-L-arginyl-L-phenylalanyl-L-valyl-L-histidyl-L-arginyl-L-prolyl-L-histidyl-L-valyl-L-.alpha.-glutamyl-L-seryl-L-glutamyl]-L-lysyl-L-norleucyl]-L-lysyl- (9CI)
(CA INDEX NAME)

CI MAN

SQL 76,21,21,17,17

SEQ 1 CSSTVSRVPW TAWAFHGYKX K
=====

HITS AT: 4-18

SEQ 1 CSSTVSRVPW TAWAFHGYKX K
=====

HITS AT: 4-18

SEQ 1 CSSLVRRFVH RPHVESQ

SEQ 1 CSSLVRRFVH RPHVESQ

REFERENCE 1: 136:117369

L4 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 390747-44-1 REGISTRY

CN L-Norleucine, N2,N6-bis[L-threonyl-L-valyl-L-seryl-L-arginyl-L-valyl-L-prolyl-L-tryptophyl-L-threonyl-L-alanyl-L-tryptophyl-L-alanyl-L-phenylalanyl-L-histidylglycyl-L-tyrosyl-N6-(L-arginyl-L-seryl-L-tyrosyl-L-glutamyl-L-histidyl-L-.alpha.-aspartyl-L-leucyl-L-arginyl-L-alanyl-L-tyrosylglycyl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-leucyl)-L-lysyl-L-norleucyl]-L-lysyl- (9CI) (CA INDEX NAME)

CI MAN

SQL 66,19,17,15,15

SEQ 1 TVSRVPWTAW AFHGYKXKX
=====

HITS AT: 1-15

SEQ 1 TVSRVPWTAW AFHGYKX
=====

HITS AT: 1-15

09/613092

SEQ 1 RSYQHDLRAY GFWRL

=====

HITS AT: 1-15

SEQ 1 RSYQHDLRAY GFWRL

=====

HITS AT: 1-15

REFERENCE 1: 136:117369

L4 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 390747-42-9 REGISTRY

CN L-Norleucine, N2,N6-bis[N-(1-oxohexadecyl)-L-cysteinyl-L-seryl-L-seryl-L-threonyl-L-valyl-L-seryl-L-arginyl-L-valyl-L-prolyl-L-tryptophyl-L-threonyl-L-alanyl-L-tryptophyl-L-alanyl-L-phenylalanyl-L-histidylglycyl-L-tyrosyl-N6-[N-(1-oxohexadecyl)-L-cysteinyl-L-seryl-L-seryl-L-arginyl-L-seryl-L-tyrosyl-L-glutaminyl-L-histidyl-L-.alpha.-aspartyl-L-leucyl-L-arginyl-L-alanyl-L-tyrosylglycyl-L-phenylalanyl-L-tryptophyl-L-arginyl-L-leucyl]-L-lysyl-L-norleucyl]-L-lysyl- (9CI) (CA INDEX NAME)

CI MAN

SQL 78,21,21,18,18

SEQ 1 CSSTVSRVPW TAWAFHGYKX K

=====

HITS AT: 4-18

SEQ 1 CSSTVSRVPW TAWAFHGYKX K

=====

HITS AT: 4-18

SEQ 1 CSSRSYQHDL RAYGFWRL

=====

HITS AT: 4-18

SEQ 1 CSSRSYQHDL RAYGFWRL

=====

HITS AT: 4-18

REFERENCE 1: 136:117369

L4 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 301300-55-0 REGISTRY

CN L-Glutamine, N-(1-oxododecyl)-L-cysteinyl-L-tyrosylglycylglycyl-L-leucyl-L-valyl-L-arginyl-L-arginyl-L-phenylalanyl-L-valyl-L-histidyl-L-arginyl-L-arginyl-L-prolyl-L-histidyl-L-valyl-L-.alpha.-glutamyl-L-seryl- (9CI) (CA INDEX NAME)

SQL 19

SEQ 1 CYGGLVRRFV HRRPHVESQ

=====

HITS AT: 5-19

REFERENCE 1: 133:295042

L4 ANSWER 8 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 241814-53-9 REGISTRY

Searcher : Shears 308-4994

09/613092

CN L-Glutamine, L-leucyl-L-valyl-L-arginyl-L-arginyl-L-phenylalanyl-L-valyl-L-histidyl-L-arginyl-L-arginyl-L-prolyl-L-histidyl-L-valyl-L-.alpha.-glutamyl-L-seryl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 3: PN: WO0204497 SEQID: 7 claimed protein

SQL 15

SEQ 1 LVRRFVHRRP HVESQ

=====

HITS AT: 1-15

REFERENCE 1: 136:117369

REFERENCE 2: 131:198616

L4 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 241814-52-8 REGISTRY

CN L-Leucine, L-arginyl-L-seryl-L-tyrosyl-L-glutaminyl-L-histidyl-L-.alpha.-aspartyl-L-leucyl-L-arginyl-L-alanyl-L-tyrosylglycyl-L-phenylalanyl-L-tryptophyl-L-arginyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2: PN: WO0204497 SEQID: 6 claimed protein

SQL 15

SEQ 1 RSYQHDLRAY GFWRL

=====

HITS AT: 1-15

REFERENCE 1: 136:117369

REFERENCE 2: 131:198616

L4 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2002 ACS

RN 241814-51-7 REGISTRY

CN L-Tyrosine, L-threonyl-L-valyl-L-seryl-L-arginyl-L-valyl-L-prolyl-L-tryptophyl-L-threonyl-L-alanyl-L-tryptophyl-L-alanyl-L-phenylalanyl-L-histidylglycyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1: PN: WO0204497 SEQID: 5 claimed protein

SQL 15

SEQ 1 TVSRVPWTAW AFHGY

=====

HITS AT: 1-15

REFERENCE 1: 136:117369

REFERENCE 2: 131:198616

~~FILE HCAPLUS~~ ENTERED AT 12:35:29 ON 15 AUG 2002

L15 49 SEA FILE=HCAPLUS ABB=ON PLU=ON PSAA(S)PNEUMOC? OR PNEUMOC? SURFACE(W) (ANTIGEN OR ADHES?) OR PNEUMON?(10A) (3 7KD? OR 37KILOD? OR 37(W) (KD? OR KILOD? OR KILO(W) (D OR DALTON OR DA)))

L16 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L15 AND (MOAB OR MAB OR MONOCLON? OR 4E9 OR 1B6 OR 8G12 OR 6F6 OR 1E7)

L17 6 L16 NOT L2

-key terms

Searcher : Shears 308-4994

09/613092

L17 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:923825 HCAPLUS

DOCUMENT NUMBER: 136:68686

TITLE: Use of coiled-coil structural scaffold to generate structure-specific peptides

INVENTOR(S): Houston, Michael E.; Hodges, Robert S.

PATENT ASSIGNEE(S): Cytovax Biotechnologies, Inc., Can.

SOURCE: PCT Int. Appl., 99 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096368	A2	20011220	WO 2001-US19168	20010614
WO 2001096368	A3	20020502		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2000-211892P P 20000614

US 2000-213387P P 20000623

AB This invention relates to the use of a coiled-coil structural scaffold to generate structure-specific peptides, including synthetic peptides derived from naturally occurring proteins of various origin. The structure of the synthetic peptides utilizes a scaffold of heptad repeat units into which epitopes from coiled-coil regions of native proteins are spliced. In particular, the synthetic peptides may be based on microbial proteins, esp. surface proteins, which occur naturally in the coiled-coil form such as pneumococcal surface proteins A and C. The synthetic peptides are immunogenic and can be used to elicit an immune response in an animal. Accordingly, they are useful as vaccines or to stimulate antibody prodn. or cell-mediated immunity to the naturally occurring protein.

L17 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:436611 HCAPLUS

DOCUMENT NUMBER: 131:86646

TITLE: Baculovirus expression, purification, and evaluation of recombinant **pneumococcal surface adhesin A** of *Streptococcus pneumoniae*

AUTHOR(S): De, B. K.; Sampson, J. S.; Ades, E. W.; Johnson, S. E.; Stinson, A. R.; Crook, J.; Tharpe, J. A.; Huebner, R. C.; Carlone, G. M.

CORPORATE SOURCE: Division Bacterial Mycotic Diseases, Centers Disease Control Prevention, National Center

Searcher : Shears 308-4994

09/613092

SOURCE: Infectious Diseases, Atlanta, GA, 30333, USA
Pathobiology (1999), 67(3), 115-122
CODEN: PATHEF; ISSN: 1015-2008
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Pneumococcal surface adhesin A (PsaA)**, with a mol. mass of 37 kD by SDS-PAGE, is a common surface protein expressed by all 90 serotypes of *S. pneumoniae*. *S. pneumoniae* serotype 6B genomic DNA was amplified to generate a DNA fragment carrying the full-length *psaA* sequence and was cloned into a baculovirus expression system. The authors expressed either cell-assocd. or cell-free nonfusion PsaA polypeptides using 2 insect cell lines, *Spodoptera frugiperda* (Sf9) and *Trichoplusia ni* 5B1-4 (High-Five). Recombinant PsaA (rPsaA) polypeptides were partially purified by partitioning in PBS/Triton X-114 buffers and by weakly basic ion exchange filter chromatog. Membrane-bound "hydrophobic rPsaA" (hrPsaA) expressed by either Sf9 or High-Five cells had a mol. mass of 38 kD by SDS-PAGE and partitioned in a Triton X-114 phase, it reacted with both rabbit polyclonal and 5 **monoclonal** anti-PsaA antibodies by dot blot or Western blot. High-Five-cell-expressed "sol. rPsaA" (srPsaA) with a mol. mass of 37 kD by SDS-PAGE, was isolated from the serum-free culture medium and did not partition in the Triton X-114 phase; it reacted with anti-PsaA rabbit polyclonal and mouse **monoclonal** antibodies by ELISA and Western blot. Both rPsaA polypeptide forms were immunogenic in adult mice. In an infant mouse model of bacteremia, survival rates for mice given mouse anti-rPsaA immune serum (from mice immunized with High-Five-expressed srPsaA; 20 .mu.l, 1:50,000 titer) 24 h before bacteremic challenge were greater than for the control group (48 h post-challenge, 20 vs. 90% survival rates) when challenged with *S. pneumoniae* serotype 6B. These results indicate that rPsaA is immunogenic and elicits protective antibody in mice similar to native protein.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L17 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:21723 HCAPLUS
DOCUMENT NUMBER: 130:77112
TITLE: *Streptococcus pneumoniae* 37-
kDa surface adhesin A protein and its
gene
INVENTOR(S): Sampson, Jacquelyn S.; Russell, Harold; Tharpe,
Jean A.; Ades, Edwin W.; Carlone, George M.
PATENT ASSIGNEE(S): United States Dept. of Health and Human
Services, USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No.
222,179, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Searcher : Shears 308-4994

09/613092

US 5854416	A	19981229	US 1996-715131	19960917
US 5422427	A	19950606	US 1991-791377	19911114
US 6312944	B1	20011106	US 1994-356106	19941215
US 6217884	B1	20010417	US 1998-221753	19981228

PRIORITY APPLN. INFO.:

US 1991-791377	A2	19911114
US 1994-222179	B2	19940404
US 1996-715131	A3	19960917

AB The invention provides a nucleic acid encoding the 37-kDa protein from *Streptococcus pneumoniae*. Also provided are isolated nucleic acids comprising a unique fragment of at least 10 nucleotides of the 37-kDa protein. The invention also provides purified polypeptides encoded by the nucleic acid encoding the 37-kDa protein from and the nucleic acids comprising a unique fragment of at least 10 nucleotides of the 37-kDa protein. Also provided are antibodies which selectively binds the polypeptides encoded by the nucleic acid encoding the 37-kDa protein and the nucleic acids comprising a unique fragment of at least 10 nucleotides of the 37-kDa protein. Also provided are vaccines comprising immunogenic polypeptides encoded by the nucleic acid encoding the 37-kDa protein and the nucleic acids comprising a unique fragment of at least 10 nucleotides of the 37-kDa protein. Further provided is a method of detecting the presence of *Streptococcus pneumoniae* in a sample comprising the steps of contacting a sample suspected of contg. *Streptococcus pneumoniae* with nucleic acid primers capable of hybridizing to a nucleic acid comprising a portion of the nucleic acid encoding the 37-kDa protein, amplifying the nucleic acid and detecting the presence of an amplification product, the presence of the amplification product indicating the presence of *Streptococcus pneumoniae* in the sample. Further provided are methods of detecting the presence of *Streptococcus pneumoniae* in a sample using antibodies or antigens, methods of preventing and treating *Streptococcus pneumoniae* infection in a subject.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:234181 HCAPLUS

DOCUMENT NUMBER: 128:307320

TITLE: Immunoreactivity of five monoclonal antibodies against the 37-kilodalton common cell wall protein (PsaA) of *Streptococcus pneumoniae*

AUTHOR(S): Crook, Jennifer; Tharpe, Jean A.; Johnson, Scott E.; Williams, Derrick B.; Stinson, Annie R.; Facklam, Richard R.; Ades, Edwin W.; Carlone, George M.; Sampson, Jacquelyn S.

CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, Atlanta, GA, 30333, USA

SOURCE: Clinical and Diagnostic Laboratory Immunology (1998), 5(2), 205-210
CODEN: CDIMEN; ISSN: 1071-412X

PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal

Searcher : Shears 308-4994

09/613092

LANGUAGE: English

AB Five **monoclonal** antibodies (**MAbs**) were produced against the *Streptococcus pneumoniae* **pneumococcal surface adhesin A (PsaA) 37-kDa** common cell wall protein. These antibodies were used in a dot immunoblot and Western blot study of clin. isolates of *S. pneumoniae* to detect the presence of the protein. By both assays, the **MAbs** reacted with clin. isolates representing the 23 type-specific serotypes present in the licensed pneumococcal polysaccharide vaccine. Western blot anal. confirmed the presence of a protein migrating in the gel with a mol. mass of 37 kDa. An extension of the study by using dot immunoblot anal. that included an anal. of the 90 serotypes of *S. pneumoniae* showed that all five **MAbs** reacted with 89 of the 90 serotypes tested. **Mab 1B6**, the exception, did not react with *S. pneumoniae* serotype 16F. Dot immunoblot anal. of the **MAbs** with *Enterococcus faecalis* and *viridans streptococci* showed varied reactivity patterns, depending on the species. The **MAbs** against the 37-kDa antigen did not react with *Escherichia coli*, respiratory pathogens, or nonpathogens representing 22 genera and 29 species of bacteria. All five **MAbs** also reacted with five multidrug-resistant strains of *S. pneumoniae*. In summary, these **MAbs** may be useful for detection of pneumococcal antigen and may lead to the development of diagnostic assays for pneumococcal disease.

L17 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:484857 HCAPLUS

DOCUMENT NUMBER: 127:175018

TITLE: Immunologic epitope, gene, and immunity involved in pneumococcal glycoconjugate

AUTHOR(S): Lee, Chi-Jen; Wang, Theresa R.; Tai, Stanley S.

CORPORATE SOURCE: Center for Biologics Evaluation and Research, Food and Drug Administration, Rockville, MD, 20852-1448, USA

SOURCE: Critical Reviews in Microbiology (1997), 23(2), 121-142

CODEN: CRVMAC; ISSN: 1040-841X

PUBLISHER: CRC

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 131 refs. Pneumococcal infection persists as a major cause of pneumonia, otitis media, and meningitis in infants. Children less than 2 yr of age show the highest incidence of pneumococcal diseases. Prodn. of **monoclonal** antibody (**Mab**) to polysaccharide (PS) and binding characteristics to PS epitopes were studied. Removal of the O-acetyl group from 9V PS by alkali hydrolysis resulted in a decreased binding with rabbit 9V antiserum (AS). However, the binding reaction with 9V **Mab** was less affected by the loss of O-acetyl content. Type 9V IgG **Mab** provided passive protection and enhanced the opsonophagocytic activity of polymorphonuclear (PMN) leukocytes to kill type 9V pneumococci. The pathogenicity of **pneumococci** is attributed to various virulence factors distributed on the cell surface, including capsular polysaccharide and protein antigens, for example, pneumolysin, autolysin, **pneumococcal surface protein A (PspA)**, **pneumococcal surface adhesion (PsaA)**, and hemin binding protein. Some

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of these protein antigens may be used as a component to combine with pneumococcal PS vaccine or as a carrier of conjugate vaccine. Clin. trials of pneumococcal conjugate vaccines showed that covalent linkage of capsular PS to protein carriers improved the immunogenicity of the PS. Development of glycoconjugate vaccine for selected pneumococcal types will help solve the problem of poor immunogenicity of PS vaccine in young children used for prevention of pneumococcal infection.

L17 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:464916 HCAPLUS

DOCUMENT NUMBER: 119:64916

TITLE: Molecular cloning of mammalian *Pneumocystis carinii* surface antigens and their use for the detection of same

INVENTOR(S): Fishman, Jay A.

PATENT ASSIGNEE(S): General Hospital Corp., USA

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
WO 9307274	A1	19930415	WO 1992-US8328	19920930
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
US 5442050	A	19950815	US 1991-781034	19911018
AU 9228691	A1	19930503	AU 1992-28691	19920930
PRIORITY APPLN. INFO.:			US 1991-768166	19910930
			US 1991-781034	19911018
			WO 1992-US8328	19920930

AB The cDNA for the gp116 major surface antigen of mammalian (rodents and human) *Pneumocystis carinii* is cloned. A .lambda.gt11 cDNA library prepd. from rat *P. carinii* was screened with **monoclonal** antibodies to obtain a pos. clone JFB1g10. This clone contained a 2814-bp cDNA insert that included an 1197-bp open reading frame encoding an unglycosylated peptide of about 44 kDa. The primers derived from rat *P. carinii* were used to amplify the gene from *P. carinii* derived from human bronchoalveolar lavage. The results showed that the sequence of the human *P. carinii* was identical to that of the rat *P. carinii* over the entire 2756 bp including the open reading frames. The sequences of rat *P. carinii* from 2 other clones were also shown. Methods for detection, prevention, and treatment of infection by *P. carinii*, that are assocd. with the cloning of the gene were also claimed.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXCENTER, PHIC, PHIN' ENTERED AT 12:52:46 ON 15 AUG 2002)

~~L18~~ 24 S L16

~~L19~~ 12 DUP REM L18 (12 DUPLICATES REMOVED)

L19 ANSWER 1 OF 12 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-195762 [25] WPIDS

DOC. NO. CPI: C2002-060493

TITLE: New multiple antigenic peptide for immunizing

Searcher : Shears 308-4994

09/613092

against streptococcal infections, binds to
monoclonal antibody obtained in response to
immunizing an animal with **pneumococcal**
surface adhesion protein A or its
fragment.

DERWENT CLASS: B04 D16
INVENTOR(S): ADES, E W; CARLONE, G M; JOHNSON, S E; JUE, D L;
SAMPSON, J S
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002004497	A2	20020117	(200225)*	EN	85
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC					
MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ					
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE					
KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO					
NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ					
VN YU ZA ZW					
AU 2001071935	A	20020121	(200234)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002004497	A2	WO 2001-US21626	20010710
AU 2001071935	A	AU 2001-71935	20010710

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001071935	A Based on	WO 200204497

PRIORITY APPLN. INFO: US 2000-613092 20000710

AN 2002-195762 [25] WPIDS

AB WO 200204497 A UPAB: 20020418

NOVELTY - A multiple antigenic peptide (I) that immunospecifically binds to a **monoclonal** antibody obtained in response to immunizing an animal with *Streptococcus pneumoniae* **pneumococcal surface adhesion** protein A (**PsaA**) or its immunogenic fragment, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for conferring protective immunity against *S. pneumoniae* infection in a subject comprising administering a therapeutic composition containing (I).

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - Vaccine. (I) was tested for protection against challenge with a virulent capsular type 3 *S. pneumoniae* strain, WU2. Twenty CB A/CaHN/J mice carrying the xid mutation (x-linked immunodeficiency) were anesthetized and bled infraorbitally to obtain pre-immunization sera. A 37 kDa protein (**pneumococcal surface adhesion** A) was emulsified in complete Freund's adjuvant (CFA) to a protein concentration of 54 micro g/ml. Ten mice were injected

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subcutaneously into 2 axillary and 2 lingual sites at 0.1 ml/site, delivering approximately 22 micro g protein/mouse. Ten control mice were treated identically with CFA and buffer substituting for protein. Fourteen days later, the 10 test mice were injected intraperitoneally (IP) with 100 micro g of the 37 kDa protein and controls were injected IP with buffer. Eight days following the IP immunizations, all mice were bled infraorbitally to obtain post-immunization sera, and challenged intravenously (IV) with 60 colony forming units (cfu) of a log phase culture of *S. pneumoniae* strain WU2. Mice were observed for 21 days, and deaths were recorded. Sera were collected prior to immunizations to establish baseline exposures, and also following the full immunization protocol in order to correlate circulating antibody to the 37 kDa protein with protection. Results showed that 10/10 mice immunized with 37 kDa protein survived and 2/10 mice (controls) with no protein survived (8/10 died).

USE - (I) is useful for conferring protective immunity against *S. pneumoniae* infection in a subject (claimed).
Dwg.0/4

L19 ANSWER 2 OF 12 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002128828 MEDLINE
DOCUMENT NUMBER: 21853521 PubMed ID: 11865401
TITLE: Inhibition of pneumococcal carriage in mice by subcutaneous immunization with peptides from the common surface protein **pneumococcal surface adhesin a**.
AUTHOR: Johnson Scott E; Dykes Janet K; Jue Danny L; Sampson Jaquelyn S; Carlone George M; Ades Edwin W
CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Respiratory Diseases Branch, Atlanta, Georgia 30333, USA.. sjohnson@cdc.gov
SOURCE: JOURNAL OF INFECTIOUS DISEASES, (2002 Feb 15) 185 (4) 489-96.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020227
Last Updated on STN: 20020317
Entered Medline: 20020315

AB **Pneumococcal surface adhesin A (PsaA)**, a common protein expressed on all 90 **pneumococcal** serotypes, is a vaccine candidate. Three anti-**PsaA monoclonal** antibody phage display-expressed mono-peptides (15 mers), in various formulations as lipidated or nonlipidated multiantigenic peptides or as bi- or tripeptide constructs, were studied in a mouse nasopharyngeal carriage model to determine the inhibitory effect of induced antibodies on carriage of **pneumococcal** serotypes 2, 4, and 6B. Antibodies to each of the various peptides tested reduced carriage of the 3 serotypes. Reduction in carriage by nonlipidated multiantigenic peptide antibodies was highly variable (39%-94%; mean, 59%; standard deviation [SD], 20.2%); however, more-consistent results were observed in mice immunized with lipidated (56%-98%; mean, 69%; SD,

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13.6%) and combination or bipeptide (55%-91%; mean, 76%; SD, 13.1%) formulations. These peptides are immunogenic, and their induced antibodies reduce carriage in mice. **PsaA** peptides demonstrate potential for being important new vaccines against **pneumococcal** carriage, otitis media, and invasive **pneumococcal** disease.

L19 ANSWER 3 OF 12 MEDLINE
ACCESSION NUMBER: 2001485546 MEDLINE
DOCUMENT NUMBER: 21418906 PubMed ID: 11527799
TITLE: Identification of the **psaA** gene, coding for **pneumococcal surface adhesin A**, in viridans group streptococci other than *Streptococcus pneumoniae*.
AUTHOR: Jado I; Fenoll A; Casal J; Perez A
CORPORATE SOURCE: Laboratorio de Referencia de Neumococos, Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Majadahonda E-28220, Madrid, Spain.
SOURCE: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (2001 Sep) 8 (5) 895-8.
Journal code: 9421292. ISSN: 1071-412X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF248229; GENBANK-AF248230; GENBANK-AF248235; GENBANK-AF248236; GENBANK-AF248237
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010903
Last Updated on STN: 20020122
Entered Medline: 20011204

AB The gene encoding the **pneumococcal surface adhesin A (PsaA)** protein has been identified in three different viridans group streptococcal species. Comparative studies of the **psaA** gene identified in different **pneumococcal** isolates by sequencing PCR products showed a high degree of conservation among these strains. **PsaA** is encoded by an open reading frame of 930 bp. The analysis of this fragment in *Streptococcus mitis*, *Streptococcus oralis*, and *Streptococcus anginosus* strains revealed a sequence identity of 95, 94, and 90%, respectively, to the corresponding open reading frame of the previously reported *Streptococcus pneumoniae* serotype 6B strain. Our results confirm that **psaA** is present and detectable in heterologous bacterial species. The possible implications of these results for the suitability and potential use of **PsaA** in the identification and diagnosis of **pneumococcal** diseases are discussed.

L19 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:223227 BIOSIS
DOCUMENT NUMBER: PREV200200223227
TITLE: Neutralization of attachment of *Streptococcus pneumoniae* to human epithelial cells by recombinant **PsaA** and anti-**PsaA** antibodies.
AUTHOR(S): Pilishvili, T. (1); Sampson, J. (1); Johnson, S. E. (1); Stinson, A. (1); Carlone, G. M. (1); Ades, E. (1); Romero-Steiner, S. (1)
CORPORATE SOURCE: (1) Centers for Disease Control and Prevention,

Searcher : Shears 308-4994

09/613092

SOURCE: Atlanta, GA USA
Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 346.
<http://www.asmta.org/mtgsrc/generalmeeting.htm>.
print.
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001
ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The attachment of **pneumococcus** (Pnc) to host cells is not well defined. We examined a neutralization of attachment assay and evaluated the role of Pnc surface adhesin A (**PsaA**) in Pnc (serotypes 6A, 6B, 19F, and 23F) attachment to Detroit 562 nasopharyngeal human epithelial cells. **PsaA** is a putative Pnc adhesin and a common protein vaccine candidate. Anti-**PsaA** antibodies (Ab) reduce Pnc colonization and carriage in mice and protect chinchillas from Pnc otitis media. A rabbit polyclonal (Pab) anti-recombinant **PsaA** (rPsaA) serum, a purified mouse anti-**PsaA** monoclonal antibody (**Mab** 6F62G8E12) and normal adult sera (n=20) with known ELISA anti-**PsaA** IgG levels were evaluated for their ability to inhibit Pnc attachment to confluent monolayers. The % inhibition of attachment by anti-**PsaA** Ab and/or rPsaA was compared to uninhibited controls that were quantified by CFU counts. Pnc attachment was dependent on capsular phenotype (no attachment for opaque strains). With an inoculum of 104 bact/well, the mean control count was 170 CFU/well (CV=20%) for transparent strains. Low attachment (mean=23 CFU at 106 bact/well) was observed for a **PsaA** minus mutant. Mean % inhibitions of attachment with Pab and **Mab** were 70 and 53%, respectively. Adult sera showed inhibition in a dose response fashion with the range of 100% to 10%, depending on the serum anti-**PsaA** antibody levels. Absorbtion of Pab and **Mab** with rPsaA restored Pnc attachment to control levels. Absorbtion of sera with the **PsaA** minus mutant did not result in a decrease of neutralization activity. Additionally, 80% of Pnc attachment could be inhibited with 0.5 mug/well of rPsaA. The neutralizing effect of r-**PsaA** and anti-**PsaA** Ab on Pnc attachment to nasopharyngeal epithelial cells was demonstrated with this functional assay. Our data supports the role of **PsaA** in Pnc attachment to human cells, and that this protein is the major Pnc attachment factor. Mouse colonization studies will demonstrate if neutralizing activity correlates with in vivo protection. This functional assay should be used in the evaluation of Ab elicited in response to **PsaA** vaccination.

L19 ANSWER 5 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000229325 MEDLINE
DOCUMENT NUMBER: 20229325 PubMed ID: 10768838
TITLE: Selection of an immunogenic and protective epitope of the PsaA protein of Streptococcus pneumoniae using a phage display library.
AUTHOR: Srivastava N; Zeiler J L; Smithson S L; Carlone G M; Ades E W; Sampson J S; Johnson S E; Kieber-Emmons T; Westerink M A
CORPORATE SOURCE: Department of Medicine, Medical College of Ohio,

Searcher : Shears 308-4994

09/613092

SOURCE: Toledo 43614, USA.
HYBRIDOMA, (2000 Feb) 19 (1) 23-31.
Journal code: 8202424. ISSN: 0272-457X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000810
Last Updated on STN: 20000810
Entered Medline: 20000721

AB Streptococcus pneumoniae is an important pathogen that causes disease in young and elderly individuals. The currently available polysaccharide vaccines have limited efficacy in those age groups most susceptible to **pneumococcal** infections. This study, focuses on mapping the epitopes of a surface protein of S. pneumoniae by biopanning a 15 mer phage display library using 5 different **monoclonal** antibodies (**MAbs**) against the **Pneumoccal surface adhesin A** (**PsaA**). **PsaA** is a component of the bacterial cell wall that is highly species specific and is involved in bacterial adherence and virulence. Biopanning of the phage display library reveals three distinct epitopes on the **PsaA** protein. The sequence homology of these epitopes ranges from two to six amino acids when compared to the native **PsaA** protein type 2. Two of these epitopes have been evaluated for their immunogenicity in mice. The peptide selected by the **MAbs 8G12, 6F6, and 1B7** is referred to as the consensus peptide and is immunogenic in mice. Optimal anti-**PsaA** response is observed in mice immunized with 50microg of the consensus peptide complexed to proteosomes in 1:1 ratio. The anti-**PsaA** response is significantly lower than the response to the **PsaA** native protein. The peptide selected by **monoclonal** antibody **4E9** in its lipidated form is significantly protective in mice challenged with S. pneumoniae serotype 2 when compared to mice immunized with the native protein. These results show that the selected epitopes of **PsaA** protein are immunogenic and protective in mice. These epitopes need to be evaluated further as alternatives to currently available vaccines.

L19 ANSWER 6 OF 12 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-540849 [45] WPIDS
DOC. NO. NON-CPI: N1999-400811
DOC. NO. CPI: C1999-158062
TITLE: New peptides corresponding to Streptococcus pneumoniae PsaA, used for treating or preventing Streptococcus pneumoniae infection in a subject.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): ADES, E W; CARLONE, G M; SAMPSON, J S; THARPE, J A; WESTERINK, M A J; ZEILER, J L
PATENT ASSIGNEE(S): (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9945121	A1	19990910	(199945)*	EN	58

Searcher : Shears 308-4994

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RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9927950 A 19990920 (200007)
BR 9908476 A 20001205 (200101)
EP 1060249 A1 20001220 (200105) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9945121	A1	WO 1999-US4326	19990226
AU 9927950	A	AU 1999-27950	19990226
BR 9908476	A	BR 1999-8476	19990226
		WO 1999-US4326	19990226
EP 1060249	A1	EP 1999-908543	19990226
		WO 1999-US4326	19990226

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9927950	A Based on	WO 9945121
BR 9908476	A Based on	WO 9945121
EP 1060249	A1 Based on	WO 9945121

PRIORITY APPLN. INFO: US 1998-76565P 19980302

AN 1999-540849 [45] WPIDS

AB WO 9945121 A UPAB: 19991103

NOVELTY - Novel peptides that immunospecifically bind to a **monoclonal** antibody (**MAB**) obtained in response to immunizing an animal with *Streptococcus pneumoniae* (SP) **pneumococcal surface adhesion A** protein (**PsaA**) are claimed.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) a peptide whose sequence results from a method comprising:
 - (a) providing a library comprised of random oligonucleotides (ONs), where the ONs are about 30-45 nucleotides in length;
 - (b) splicing the ONs of the library into the gene for the gene III coat protein of a filamentous bacteriophage in frame with the codons for the amino acid residues of the coat protein, where the gene for the gene III coat protein is contained within the bacteriophage genome, thereby creating bacteriophage library, and where the ONs are positioned within the gene such that when the coat protein is expressed and incorporated into a complete bacteriophage particle, the peptide is available as an epitope to which an antibody can bind;
 - (c) expanding the bacteriophage library harboring the ON library by culturing the bacteriophage library in a host which the bacteriophage infects;
 - (d) screening the expanded bacteriophage library for a specific bacteriophage particle that immunospecifically reacts with a **MAB** obtained in response to immunizing an animal with SP

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PsaA; and

(e) sequencing the gene for the coat protein of the specific bacteriophage particle obtained in (d) thereby yielding the nucleotide sequence of that member of the ON library whose translation product has the sequence of the peptide potentially capable of eliciting protective immunity against SP;

(2) a therapeutic composition comprising one or more peptides that immunospecifically bind to a **MAb** obtained in response to immunizing an animal with SP PsaA, and an immunostimulatory carrier, where the therapeutic composition confers protective immunity against SP infection when administered to a subject;

(3) a peptide comprising a sequence which is at least 80% identical to a peptide whose sequence is chosen from sequences (V) - (VIII) or immunogenic fragments:

Sequence (V): Thr Val Ser Arg Val Pro Trp Thr Ala Trp Ala Phe His Gly Tyr;

Sequence (VI): Arg Ser Tyr Gln His Asp Leu Arg Ala Tyr Gly Phe Trp Arg Leu;

Sequence (VII): Leu Val Arg Arg Phe Val His Arg Arg Pro His Val Glu Ser Gln;

Sequence (VIII): Leu Val Arg Arg Phe Val His His Arg Pro His Val Glu Ser Gln.

USE - The peptides can be used for treating or preventing infection by SP in a subject.

Dwg.0/0

L19 ANSWER 7 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:325906 BIOSIS

DOCUMENT NUMBER: PREV199900325906

TITLE: Immunologic characterization of a **monoclonal** antibody to *Streptococcus pneumoniae* **pneumococcal surface adhesin A (PsaA)** protein.

AUTHOR(S): Sampson, J. S. (1); Ades, E. W. (1); Romero-Steiner, S. (1); Johnson, S. (1); Daugharty, H. (1); Dykes, J. (1); Stinson, A. (1); Crook, J. (1); Carlone, G. M. (1)

CORPORATE SOURCE: (1) CDC, Atlanta, GA USA

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1999) Vol. 99, pp. 273. Meeting Info.: 99th General Meeting of the American Society for Microbiology Chicago, Illinois, USA May 30-June 3, 1999 American Society for Microbiology . ISSN: 1060-2011.

DOCUMENT TYPE: Conference

LANGUAGE: English

L19 ANSWER 8 OF 12 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 1999323812 MEDLINE

DOCUMENT NUMBER: 99323812 PubMed ID: 10394131

TITLE: Baculovirus expression, purification and evaluation of recombinant **pneumococcal surface adhesin A** of *Streptococcus pneumoniae*.

AUTHOR: De B K; Sampson J S; Ades E W; Johnson S E; Stinson A R; Crook J; Tharpe J A; Huebner R C; Carlone G M

CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA..

Searcher : Shears 308-4994

09/613092

SOURCE: bkd1@cdc.gov
PATHOBIOLOGY, (1999 May-Jun) 67 (3) 115-22.
Journal code: 9007504. ISSN: 1015-2008.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991014
Last Updated on STN: 19991014
Entered Medline: 19991001

AB **Pneumococcal surface adhesin A (PsaA)**, with a molecular mass of approximately 37 kD by SDS-PAGE, is a common surface protein expressed by all 90 serotypes of *Streptococcus pneumoniae*. *S. pneumoniae* serotype 6B genomic DNA was amplified to generate a DNA fragment carrying the full-length **psaA** sequence and was cloned into a baculovirus expression system. We expressed either cell-associated or cell-free nonfusion **PsaA** polypeptides using two insect cell lines, *Spodoptera frugiperda* (Sf9) and *Trichoplusia ni* 5B1-4 (High-Five). Recombinant **PsaA** (rPsaA) polypeptides were partially purified by partitioning in PBS/Triton X-114 buffers and by weakly basic ion exchange filter chromatography. Membrane-bound 'hydrophobic rPsaA' (hrPsaA) expressed by either Sf9 or High-Five cells had a molecular mass of approximately 38 kD by SDS-PAGE and partitioned in a Triton X-114 phase, it reacted with both rabbit polyclonal and five **monoclonal** anti-**PsaA** antibodies by dot blot or Western blot analysis. High-Five-cell-expressed 'soluble rPsaA' (srPsaA) with a molecular mass of approximately 37 kD by SDS-PAGE, was isolated from the serum-free culture medium and did not partition in the Triton X-114 phase; it reacted with anti-**PsaA** rabbit polyclonal and mouse **monoclonal** antibodies by ELISA and Western blot analysis. Both rPsaA polypeptide forms were immunogenic in Swiss-Webster adult female mice. In an infant mouse model of bacteremia, survival rates for mice given mouse anti-rPsaA immune serum (from mice immunized with High-Five-expressed srPsaA; 20 µg/ml, 1:50,000 titer) 24 h before bacteremic challenge were greater than for the control group (48 h postchallenge, 20 vs. 90% survival rates) when challenged with *S. pneumoniae* serotype 6B. These results indicate that rPsaA is immunogenic and elicits protective antibody in mice similar to native protein.

L19 ANSWER 9 OF 12 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1998180439 MEDLINE
DOCUMENT NUMBER: 98180439 PubMed ID: 9521144
TITLE: Immunoreactivity of five **monoclonal** antibodies against the 37-kilodalton common cell wall protein (PsaA) of *Streptococcus pneumoniae*.
AUTHOR: Crook J; Tharpe J A; Johnson S E; Williams D B; Stinson A R; Facklam R R; Ades E W; Carlone G M; Sampson J S
CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.
SOURCE: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (1998 Mar) 5 (2) 205-10.

Searcher : Shears 308-4994

09/613092

JOURNAL code: 9421292. ISSN: 1071-412X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980609
Last Updated on STN: 19980609
Entered Medline: 19980526

AB Five **monoclonal** antibodies (**MAbs**) were produced against the *Streptococcus pneumoniae* **pneumococcal surface adhesin A (PsaA) 37-kDa** common cell wall protein. These antibodies were used in a dot immunoblot and Western blot study of clinical isolates of *S. pneumoniae* to detect the presence of the protein. By both assays, the **MAbs** reacted with clinical isolates representing the 23 type-specific serotypes present in the licensed **pneumococcal** polysaccharide vaccine. Western blot analysis confirmed the presence of a protein migrating in the gel with a molecular mass of 37 kDa. An extension of the study by using dot immunoblot analysis that included an analysis of the 90 serotypes of *S. pneumoniae* showed that all five **MAbs** reacted with 89 of the 90 serotypes tested. **Mab 1B6**, the exception, did not react with *S. pneumoniae* serotype 16F. Dot immunoblot analysis of the **MAbs** with *Enterococcus faecalis* and *viridans streptococci* showed varied reactivity patterns, depending on the species. The **MAbs** against the 37-kDa antigen did not react with *Escherichia coli*, respiratory pathogens, or nonpathogens representing 22 genera and 29 species of bacteria. All five **MAbs** also reacted with five multidrug-resistant strains of *S. pneumoniae*. In summary, these **MAbs** may be useful for detection of **pneumococcal** antigen and may lead to the development of diagnostic assays for **pneumococcal** disease.

L19 ANSWER 10 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:282905 BIOSIS

DOCUMENT NUMBER: PREV199799582108

TITLE: Immunoreactivity of five **monoclonal** antibodies against the 37-kilodalton common cell-wall protein of *Streptococcus pneumoniae*.

AUTHOR(S): Crook, J.; Tharpe, J.; Johnson, S.; Williams, D.; Stinson, A.; Carlone, G.; Ades, E.; Sampson, J.

CORPORATE SOURCE: Cent. Disease Control Prevention, Atlanta, GA USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1997) Vol. 97, No. 0, pp. 234.

Meeting Info.: 97th General Meeting of the American Society for Microbiology Miami Beach, Florida, USA May 4-8, 1997
ISSN: 1060-2011.

DOCUMENT TYPE: Conference; Abstract; Conference

LANGUAGE: English

L19 ANSWER 11 OF 12 MEDLINE

DUPLICATE 5

ACCESSION NUMBER: 97369652 MEDLINE

DOCUMENT NUMBER: 97369652 PubMed ID: 9226111

Searcher : Shears 308-4994

09/613092

TITLE: Immunologic epitope, gene, and immunity involved in pneumococcal glycoconjugate.
AUTHOR: Lee C J; Wang T R; Tai S S
CORPORATE SOURCE: Center for Biologics Evaluation and Research, Food and Drug Administration, Rockville, Maryland 20852-1448, USA.
SOURCE: CRITICAL REVIEWS IN MICROBIOLOGY, (1997) 23 (2) 121-42. Ref: 131
Journal code: 8914274. ISSN: 1040-841X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970916
Last Updated on STN: 19970916
Entered Medline: 19970904

AB **Pneumococcal** infection persists as a major cause of pneumonia, otitis media, and meningitis in infants. Children less than 2 years of age show the highest incidence of **pneumococcal** diseases. Production of **monoclonal** antibody (**MAB**) to polysaccharide (PS) and binding characteristics to PS epitopes were studied. Removal of the O-acetyl group from 9V PS by alkali hydrolysis resulted in a decreased binding with rabbit 9V antiserum (AS). However, the binding reaction with 9V **MAB** was less affected by the loss of O-acetyl content. Type 9V IgG **MAB** provided passive protection and enhanced the opsonophagocytic activity of polymorphonuclear (PMN) leukocytes to kill type 9V **pneumococci**. The pathogenicity of **pneumococci** is attributed to various virulence factors distributed on the cell surface, including capsular polysaccharide and protein antigens, for example, pneumolysin, autolysin, **pneumococcal** surface protein A (PspA), **pneumococcal** surface adhesion (PsaA), and hemin binding protein. Some of these protein antigens may be used as a component to combine with **pneumococcal** PS vaccine or as a carrier of conjugate vaccine. Clinical trials of **pneumococcal** conjugate vaccines showed that covalent linkage of capsular PS to protein carriers improved the immunogenicity of the PS. Development of glycoconjugate vaccine for selected **pneumococcal** types will help solve the problem of poor immunogenicity of PS vaccine in young children used for prevention of **pneumococcal** infection.

L19 ANSWER 12 OF 12 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 91035919 MEDLINE
DOCUMENT NUMBER: 91035919 PubMed ID: 2229341
TITLE: **Monoclonal** antibody recognizing a species-specific protein from Streptococcus pneumoniae.
AUTHOR: Russell H; Tharpe J A; Wells D E; White E H; Johnson J E
CORPORATE SOURCE: Division of Bacterial Diseases, Centers for Disease Control, Atlanta, Georgia 30333.
SOURCE: JOURNAL OF CLINICAL MICROBIOLOGY, (1990 Oct) 28 (10) 2191-5.

Searcher : Shears 308-4994

09/613092

JOURNAL code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199012
ENTRY DATE: Entered STN: 19910208
Last Updated on STN: 19910208
Entered Medline: 19901220

AB **Monoclonal** antibodies (**MAbs**) against a nonencapsulated strain (R36A) of *Streptococcus pneumoniae* were produced to aid in a search for antigens common to this species. By Western immunoblot analysis, a species-specific 37-kilodalton (kDa) protein was found in lysates of 24 different encapsulated strains of *S. pneumoniae*. **Monoclonal** antibodies against the 37-kDa antigen did not react with 55 heterologous strains representing 19 genera and 36 species of bacteria that can also cause acute lower respiratory tract disease. Immunogold staining suggests that the antigen is synthesized inside the pneumococcal cell. However, **MAbs** to the 37-kDa antigen bound whole cells in the enzyme-linked immunosorbent assay and the indirect immunofluorescence assay. Antibody-binding epitopes of the antigen are probably exposed on the outer surface of the pneumococcus cell wall. The effectiveness of the 37-kDa antigen as a useful diagnostic marker is under study.

~~(FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, TOXCENTER, PHIC, PHIN' ENTERED AT 12:54:42 ON 15 AUG 2002)~~

L20 654 SEA ABB=ON PLU=ON ADES E?/AU
L21 12207 SEA ABB=ON PLU=ON JOHNSON S?/AU
L22 444 SEA ABB=ON PLU=ON JUE D?/AU
L23 1417 SEA ABB=ON PLU=ON SAMPSON J?/AU
L24 468 SEA ABB=ON PLU=ON CARLONE G?/AU
L25 10 SEA ABB=ON PLU=ON L20 AND L21 AND L22 AND L23 AND L24
L26 75 SEA ABB=ON PLU=ON L20 AND (L21 OR L22 OR L23 OR L24)
L27 36 SEA ABB=ON PLU=ON L21 AND (L22 OR L23 OR L24)
L28 15 SEA ABB=ON PLU=ON L22 AND (L23 OR L24)
L29 92 SEA ABB=ON PLU=ON L23 AND L24
L30 79 SEA ABB=ON PLU=ON (L20 OR L21 OR L22 OR L23 OR L24 OR L26 OR L27 OR L29) AND L15
~~L31 83 SEA ABB=ON PLU=ON L25 OR L28 OR L30~~
~~L32 34 DUP REM L31 (49 DUPLICATES REMOVED)~~

- Author (S)

L32 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:51509 HCAPLUS
DOCUMENT NUMBER: 136:117369
TITLE: Multiple antigenic peptides induce protective immune response against *Streptococcus pneumoniae*
INVENTOR(S): Ades, Edwin W.; Johnson, Scott E.; Jue, Danny L.; Sampson, Jacquelyn S.; Carlone, George M.
PATENT ASSIGNEE(S): The Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

Searcher : Shears 308-4994

09/613092

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004497	A2	20020117	WO 2001-US21626	20010710
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2000-613092 A2 20000710

AB The authors disclose the cloning and immunogenicity of the pneumococcal surface A protein (PspA) of *S. pneumoniae* challenge. In addn., the authors disclose epitope mapping for anti-PspA monoclonal antibodies obtained by panning of a phage display library. In one example, immunization of xid mice with PspA provided protective immunity against subsequent challenge. A in a second example, immunization of Balb/C mice with lipidated peptides or multiple antigenic peptide constructs were shown to inhibit bacterial colonization.

L32 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

ACCESSION NUMBER: 2002:199850 HCAPLUS

TITLE: Inhibition of pneumococcal carriage in mice by subcutaneous immunization with peptides from the common surface protein **pneumococcal surface adhesin A**

AUTHOR(S): Johnson, Scott E.; Dykes, Janet K.; Jue, Danny L.; Sampson, Jaquelyn S.; Carlone, George M.; Ades, Edwin W.

CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, 30333, USA

SOURCE: Journal of Infectious Diseases (2002), 185(4), 489-496

CODEN: JIDIAQ; ISSN: 0022-1899

PUBLISHER: University of Chicago Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Pneumococcal surface adhesin A (PsaA)**, a common protein expressed on all 90 **pneumococcal** serotypes, is a vaccine candidate. Three anti-**PsaA** monoclonal antibody phage display-expressed mono-peptides (15 mers), in various formulations as lipidated or nonlipidated multiantigenic peptides or as bi- or tripeptide constructs, were studied in a mouse nasopharyngeal carriage model to det. the inhibitory effect of induced antibodies on carriage of **pneumococcal** serotypes 2, 4, and 6B. Antibodies to each of the various peptides tested reduced carriage of the 3 serotypes.

Searcher : Shears 308-4994

09/613092

Redn. in carriage by nonlipidated multiantigenic peptide antibodies was highly variable (39%-94%; mean, 59%; std. deviation [SD], 20.2%); however, more-consistent results were obsd. in mice immunized with lipidated (56%-98%; mean, 69%; SD, 13.6%) and combination or bipeptide (55%-91%; mean, 76%; SD, 13.1%) formulations. These peptides are immunogenic, and their induced antibodies reduce carriage in mice. **PsaA** peptides demonstrate potential for being important new vaccines against **pneumococcal** carriage, otitis media, and invasive **pneumococcal** disease.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2002:274530 HCAPLUS
TITLE: Newly characterized species-specific immunogenic Chlamydophila pneumoniae peptide reactive with murine monoclonal and human serum antibodies
AUTHOR(S): Marston, Eric L.; James, Andrea V.; Parker, J. Todd; Hart, John C.; Brown, Teresa M.; Messmer, Trudy O.; Jue, Danny L.; Black, Carolyn M.; Carlone, George M.; Ades, Edwin W.; Sampson, Jacquelyn
CORPORATE SOURCE: Respiratory Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, Atlanta, GA, 30333, USA
SOURCE: Clinical and Diagnostic Laboratory Immunology (2002), 9(2), 446-452
CODEN: CDIMEN; ISSN: 1071-412X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A monoclonal antibody (MAb) directed against an unknown Chlamydophila pneumoniae epitope has been characterized, and the resp. peptide mimotope has been identified. A murine MAb specific for C. pneumoniae was used to select peptides from phage display libraries. The peptides identified from the phage display library clones reacted specifically with the resp. target murine MAb and with human sera previously identified as having antibody titers to C. pneumoniae. The selected peptide mimotope sequences tended to be composed of charged residues surrounding a core of hydrophobic residues. The peptide with the best binding could inhibit >95% of binding to the MAb, suggesting that the selected peptide binds the paratope of the resp. MAb. The peptide reacted with human sera previously detd. by microimmunofluorescence to have anti-C. pneumoniae antibodies. The peptide was competitively competed with the MAb against Renografin-purified, sonicated C. pneumoniae in an ELISA and with whole-cell C. pneumoniae in an indirect fluorescence assay format, demonstrating its potential utility in the development of diagnostics. The use of this novel peptide may allow investigators to establish standardized assays free from cross-reactive Chlamydia trachomatis and Chlamydophila psittaci epitopes and immunoreactivity.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE

09/613092

FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L32 ANSWER 4 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 4

ACCESSION NUMBER: 2001:465413 BIOSIS

DOCUMENT NUMBER: PREV200100465413

TITLE: Streptococcus pneumoniae 37-
kDa surface adhesin a protein.

AUTHOR(S): Sampson, Jacquelyn S. (1); Russell, Harold;
Tharpe, Jean A.; Ades, Edwin W.;
Carlone, George M.

CORPORATE SOURCE: (1) College Park, GA USA

ASSIGNEE: The United States of America as represented
by the Department of Health and Human Services

PATENT INFORMATION: US 6217884 April 17, 2001

SOURCE: Official Gazette of the United States Patent and
Trademark Office Patents, (Apr. 17, 2001) Vol. 1245,
No. 3, pp. No Pagination. e-file.
ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

AB The invention provides a nucleic acid encoding the 37-
kDa protein from Streptococcus pneumoniae. Also
provided are isolated nucleic acids comprising a unique fragment of
at least 10 nucleotides of the 37-kDa protein. The invention also
provides purified polypeptides encoded by the nucleic acid encoding
the 37-kDa protein from and the nucleic acids comprising a unique
fragment of at least 10 nucleotides of the 37-kDa protein. Also
provided are antibodies which selectively binds the polypeptides
encoded by the nucleic acid encoding the 37-kDa protein and the
nucleic acids comprising a unique fragment of at least 10
nucleotides of the 37-kDa protein. Also provided are vaccines
comprising immunogenic polypeptides encoded by the nucleic acid
encoding the 37-kDa protein and the nucleic acids comprising a
unique fragment of at least 10 nucleotides of the 37-kDa protein.
Further provided is a method of detecting the presence of
Streptococcus pneumoniae in a sample comprising the steps of
contacting a sample suspected of containing Streptococcus pneumoniae
with nucleic acid primers capable of hybridizing to a nucleic acid
comprising a portion of the nucleic acid encoding the 37-kDa
protein, amplifying the nucleic acid and detecting the presence of
an amplification product, the presence of the amplification product
indicating the presence of Streptococcus pneumoniae in the sample.
Further provided are methods of detecting the presence of
Streptococcus pneumoniae in a sample using antibodies or antigens,
methods of preventing and treating Streptococcus pneumoniae
infection in a subject.

L32 ANSWER 5 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:223227 BIOSIS

DOCUMENT NUMBER: PREV200200223227

TITLE: Neutralization of attachment of Streptococcus
pneumoniae to human epithelial cells by recombinant
PsaA and anti-PsaA antibodies.

AUTHOR(S): Pilishvili, T. (1); Sampson, J. (1);
Johnson, S. E. (1); Stinson, A. (1);
Carlone, G. M. (1); Ades, E. (1);

Searcher : Shears 308-4994

09/613092

CORPORATE SOURCE: Romero-Steiner, S. (1)
(1) Centers for Disease Control and Prevention,
Atlanta, GA USA
SOURCE: Abstracts of the General Meeting of the American
Society for Microbiology, (2001) Vol. 101, pp. 346.
<http://www.asmusa.org/mtgsrsrc/generalmeeting.htm>.
print.
Meeting Info.: 101st General Meeting of the American
Society for Microbiology Orlando, FL, USA May 20-24,
2001
ISSN: 1060-2011.
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The attachment of **pneumococcus** (Pnc) to host cells is not well defined. We examined a neutralization of attachment assay and evaluated the role of Pnc surface adhesin A (**PsaA**) in Pnc (serotypes 6A, 6B, 19F, and 23F) attachment to Detroit 562 nasopharyngeal human epithelial cells. **PsaA** is a putative Pnc adhesin and a common protein vaccine candidate. Anti-**PsaA** antibodies (Ab) reduce Pnc colonization and carriage in mice and protect chinchillas from Pnc otitis media. A rabbit polyclonal (Pab) anti-recombinant **PsaA** (rPsaA) serum, a purified mouse anti-**PsaA** monoclonal antibody (Mab 6F62G8E12) and normal adult sera (n=20) with known ELISA anti-**PsaA** IgG levels were evaluated for their ability to inhibit Pnc attachment to confluent monolayers. The % inhibition of attachment by anti-**PsaA** Ab and/or rPsaA was compared to uninhibited controls that were quantified by CFU counts. Pnc attachment was dependent on capsular phenotype (no attachment for opaque strains). With an inoculum of 104 bact/well, the mean control count was 170 CFU/well (CV=20%) for transparent strains. Low attachment (mean=23 CFU at 106 bact/well) was observed for a **PsaA** minus mutant. Mean % inhibitions of attachment with Pab and Mab were 70 and 53%, respectively. Adult sera showed inhibition in a dose response fashion with the range of 100% to 10%, depending on the serum anti-**PsaA** antibody levels. Absorption of Pab and Mab with rPsaA restored Pnc attachment to control levels. Absorption of sera with the **PsaA** minus mutant did not result in a decrease of neutralization activity. Additionally, 80% of Pnc attachment could be inhibited with 0.5 mug/well of rPsaA. The neutralizing effect of r-**PsaA** and anti-**PsaA** Ab on Pnc attachment to nasopharyngeal epithelial cells was demonstrated with this functional assay. Our data supports the role of **PsaA** in Pnc attachment to human cells, and that this protein is the major Pnc attachment factor. Mouse colonization studies will demonstrate if neutralizing activity correlates with in vivo protection. This functional assay should be used in the evaluation of Ab elicited in response to **PsaA** vaccination.

L32 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
ACCESSION NUMBER: 2000:900482 HCAPLUS
DOCUMENT NUMBER: 134:46755
TITLE: Pneumococcal surface protein combination vaccine
INVENTOR(S): Huebner, Robert C.; Sampson, Jacquelyn
S.; Carlone, George M.;
Ades, Edwin; Briles, David E.
PATENT ASSIGNEE(S): Uab Research Foundation, USA; Aventis Pasteur;
Centers for Disease Control and Prevention

Searcher : Shears 308-4994

09/613092

SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076541	A1	20001221	WO 2000-US40176	20000609
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
BR 2000011478	A	20020319	BR 2000-11478	20000609
EP 1189632	A1	20020327	EP 2000-947640	20000609
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.: US 1999-138422P P 19990610
US 2000-587833 A 20000606
WO 2000-US40176 W 20000609

AB The present invention relates to synergistic immunogenic combinations contg. two or more **pneumococcal** surface proteins, including PspA and/or PspC and/or **PsaA**, advantageously, PspA and **PsaA**. Also provided are methods of intranasal administration of such immunogenic combinations to reduce nasopharyngeal carriage of pneumococci and methods of use of such immunogenic combinations in the prevention and treatment of S. pneumoniae infection.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 7 OF 34 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2000165134 MEDLINE
DOCUMENT NUMBER: 20165134 PubMed ID: 10699329
TITLE: Purification and characterization of Streptococcus pneumoniae palmitoylated **pneumococcal surface adhesin A** expressed in Escherichia coli.
AUTHOR: De B K; **Sampson J S**; **Ades E W**; Huebner R C; **Jue D L**; **Johnson S E**; Espina M; Stinson A R; Briles D E; **Carlone G M**
CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases, and Biotechnology Core Facility Branch, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA.. bkd1@cdc.gov
SOURCE: VACCINE, (2000 Mar 6) 18 (17) 1811-21.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

Searcher : Shears 308-4994

09/613092

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000413

AB All *Streptococcus pneumoniae* isolates tested to date express a species-common lipoprotein designated as **pneumococcal surface adhesin A (PsaA)**. This protein is cell-associated, hydrophobic, immunogenic, and genetically conserved. It is currently under investigation as a potential component in third-generation **pneumococcal** vaccine formulations. To overcome the problem of low-level expression of native hydrophobic **PsaA** in *S. pneumoniae*, and also of the recombinant **PsaA** (rPsaA) in *Escherichia coli*, we generated a stable *E. coli* construct expressing functional palmitoylated rPsaA (approximately 10 mg/l of fermentation culture) using *Borrelia burgdorferi* outer surface protein A (OspA, a hydrophobic lipoprotein) signal peptide. By Western blot analysis, the chimeric rPsaA (approximately 34 kDa) was detected in the cell lysate using anti-**PsaA** antibodies. It was partially purified by extracting the cell pellet with PBS/Triton X(R)-114 buffers, followed by anion exchange filter chromatography. A trypsin digestion profile of rPsaA closely resembled that of the native protein, as revealed by SDS-PAGE/silver staining. Lipidation of rPsaA was confirmed by labeling recombinant *E. coli* cells with [(3)H] palmitic acid and analyzing the labeled *E. coli* cells by Western blotting coupled with autoradiography. Further, analysis of purified rPsaA by mass spectrometry (MALDI-TOF) revealed a heterogenous spectrum with a major peak (M+H)(+1) of mass 33,384 Da (theoretical mass of palmitoylated rPsaA=33,361 Da). Purified rPsaA was immunogenic in CBA/NCAHN-XID female mice following intranasal immunization with or without adjuvant, as determined by measurement of anti-**PsaA** serum IgG levels. These anti-**PsaA** antibodies reacted with both native and rPsaA polypeptides. Our data strongly suggest that *E. coli*-expressed rPsaA is palmitoylated and closely resembles the native protein in structure and immunogenicity. It was also observed to elicit measurable protection against nasopharyngeal carriage with *S. pneumoniae*.

L32 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
ACCESSION NUMBER: 2000:738306 HCAPLUS
DOCUMENT NUMBER: 134:294201
TITLE: Natural development of antibodies to
pneumococcal surface protein A,
**pneumococcal surface
adhesin A**, and pneumolysin in relation
to pneumococcal carriage and acute otitis media
AUTHOR(S): Rapola, Satu; Jantti, Virva; Haikala, Raili;
Syrjanen, Ritva; **Carlone, George M.**;
Sampson, Jacquelyn S.; Briles, David E.;
Paton, James C.; Takala, Aino K.; Kilpi, Terhi
M.; Kayhty, Helena
CORPORATE SOURCE: National Public Health Institute, Helsinki;
00300, Finland
SOURCE: Journal of Infectious Diseases (2000), 182(4),
1146-1152
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press

Searcher : Shears 308-4994

09/613092

DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Pneumococcal** surface protein A (PspA), **pneumococcal surface adhesin A (PsaA)**, and pneumolysin (Ply) are common to virtually all *Streptococcus pneumoniae* isolates. They are immunogenic and protective against pneumococcal challenge in animals and are the major candidates for a protein-based pneumococcal vaccine for humans. However, little is known of the natural development of antibodies to these proteins in humans. The objective of this study was to evaluate the natural development of antibodies to PspA, **PsaA**, and Ply in relation to **pneumococcal** infection and carriage in young children. Serum antibodies to these proteins were measured by EIA in children at ages 6, 12, 18, and 24 mo and in their mothers. All age groups were capable of producing antibodies to the 3 proteins. The antibody concns. increased with age and were strongly assocd. with pneumococcal exposure, whether by carriage or infection (acute otitis media).

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 8

ACCESSION NUMBER: 2000:81777 HCAPLUS

DOCUMENT NUMBER: 132:221053

TITLE: Intranasal immunization of mice with a mixture of the **pneumococcal** proteins **PsaA** and PspA is highly protective against nasopharyngeal carriage of *Streptococcus pneumoniae*

AUTHOR(S): Briles, David E.; **Ades, Eddie**; Paton, James C.; **Sampson, Jacquelyn S.**; **Carlone, George M.**; Huebner, Robert C.; Virolainen, Anni; Swiatlo, Edwin; Hollingshead, Susan K.

CORPORATE SOURCE: Department of Microbiology and Department of Pediatrics, University of Alabama at Birmingham, Birmingham, AL, 35294, USA

SOURCE: Infection and Immunity (2000), 68(2), 796-800
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Acquisition of pneumococci is generally from carriers rather than from infected individuals. Therefore, to induce herd immunity against *Streptococcus pneumoniae* it will be necessary to elicit protection against carriage. Capsular polysaccharide-protein conjugates, PspA, and **PsaA** are known to elicit some protection against nasopharyngeal carriage of **pneumococci** but do not always completely eliminate carriage. In this study, we obsd. that PsaA elicited better protection than did PspA against carriage. Pneumolysin elicited no protection against carriage. Immunization with a mixt. of PsaA and PspA elicited the best protection against carriage. These results indicate that PspA and PsaA may be useful for the elicitation of herd immunity in humans. As PspA and pneumolysin are known to elicit immunity to bacteremia and pneumonia, their inclusion in a mucosal vaccine may enable such a vaccine to prevent invasive disease as well as carriage.

09/613092

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L32 ANSWER 10 OF 34 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2001136240 MEDLINE
DOCUMENT NUMBER: 20539387 PubMed ID: 11089655
TITLE: Streptococcus pneumoniae serotype 4 outbreak in a
home for the aged: report and review of recent
outbreaks.
AUTHOR: Gleich S; Morad Y; Echague R; Miller J R; Kornblum J;
Sampson J S; Butler J C
CORPORATE SOURCE: Division of Infectious Diseases, St John's Episcopal
Hospital, Far Rockaway, New York 11691, USA.
SOURCE: INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY, (2000
Nov) 21 (11) 711-7. Ref: 70
Journal code: 8804099. ISSN: 0899-823X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Nursing Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301

AB OBJECTIVE: To describe a pneumonia outbreak caused by Streptococcus pneumoniae among residents of a home for the aged and to review contemporary pneumococcal outbreaks. DESIGN: Epidemiological investigation. METHODS: S pneumoniae isolates were serotyped and analyzed by pulsed-field gel electrophoresis. Paired sera were tested for antibodies to pneumococcal surface adhesin A protein (PsaA, a 37-kDa cell-wall protein). Pneumococcal outbreaks reported in the last decade in English were reviewed. RESULTS: Pneumonia developed in 18 of 200 residents. In 11 (61%), a pneumococcal etiology was demonstrated. S pneumoniae, serotype 4, was isolated from the blood cultures of 3 patients; all isolates were indistinguishable by pulsed-field gel electrophoresis. Pneumococcal involvement was established in 2 by sputum culture and latex agglutination of parapneumonic fluid and in 6 others by a twofold rise in optical density of serum antibody reactive to PsaA. Pneumococcal immunization had not previously been received by any patient; mortality was 22%. No additional cases were noted following administration of pneumococcal vaccine and antibiotic prophylaxis with penicillin or erythromycin. Twenty-six outbreaks of invasive pneumococcal disease since 1990 were reviewed. Twelve occurred in the United States, and serotypes 23F, 14, and 4 accounted for 8 (67%) of 12 outbreaks. All confirmed serotypes in US outbreaks are included in the 23-valent vaccine. More than one half of pneumococcal outbreaks worldwide involved elderly persons in hospitals or long-term-care facilities. CONCLUSIONS: A pneumococcal pneumonia outbreak occurred among unvaccinated residents of a residential facility for the aged. Institutionalized elderly persons are at risk of outbreaks of pneumococcal disease and should be vaccinated.

09/613092

L32 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 2000:74603 HCAPLUS
DOCUMENT NUMBER: 133:84850
TITLE: Confirmation of *psaA* in all 90 serotypes of
Streptococcus pneumoniae by PCR and potential of
this assay for identification and diagnosis
AUTHOR(S): Morrison, Katherine E.; Lake, Derrick; Crook,
Jennifer; **Carlone, George M.**;
Ades, Edwin; Facklam, Richard;
Sampson, Jacquelyn S.
CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases,
National Center for Infectious Diseases,
Atlanta, GA, 30333, USA
SOURCE: Journal of Clinical Microbiology (2000), 38(1),
434-437
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The gene encoding the **pneumococcal surface**
adhesin A (PsaA) protein, **psaA**, was
confirmed in all *Streptococcus pneumoniae* serotypes by a newly
developed PCR (**psaA** PCR) assay. Eighty-nine of the 90
serotypes amplified produced an 838-bp fragment; the exception was a
serotype 16F strain acquired from the American Type Culture
Collection (ATCC). Anal. of 20 addnl. 16F strains from the United
States and Brazil showed that the gene was amplified in all 16F
strains, implying that the serotype 16F ATCC strain must be a
variant. The specificity of the assay was verified by the lack of
signal from anal. of heterologous bacterial species (n = 30) and
genera (n = 14), including viridans group streptococci. The
potential of the assay for clin. application was shown by its
ability to detect pneumococci in culture-pos. nasopharyngeal
specimens. Demonstration of **psaA** in all 90 serotypes and
lack of amplification of heterologous organisms suggest that this
assay could be a useful tool for detection of **pneumococci**
and diagnosis of disease.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L32 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
ACCESSION NUMBER: 2000:719792 HCAPLUS
DOCUMENT NUMBER: 135:4254
TITLE: **Pneumococcal surface**
adhesin A antibody concentration in
serum and nasopharyngeal carriage of
Streptococcus pneumoniae in young African
infants
AUTHOR(S): Obaro, S. K.; Adegbola, R. A.; Tharpe, J. A.;
Ades, E. W.; McAdam, K. P. W. J.;
Carlone, G.; **Sampson, J. S.**
CORPORATE SOURCE: MRC Laboratories, Fajara, Banjul, Gambia
SOURCE: Vaccine (2000), 19(4-5), 411-412
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal

Searcher : Shears 308-4994

09/613092

LANGUAGE: English

AB Of the reported pneumococcal proteins, only pneumolysin and pneumococcal surface protein A (PspA) have been extensively studied for their suitability as vaccine candidates. An immunogenic 37-kDa species-common protein from *Streptococcus pneumoniae* was recently identified and designated as pneumococcal surface adhesin A (PsaA). A study was conducted to examine anti-PsaA antibody and carriage of *S. pneumoniae* from serum and nasopharyngeal swabs concurrently obtained from young infants, who had not recently been on antimicrobials, enrolled in a pneumococcal carriage study in the Upper River Division of The Gambia, West Africa. Results indicated the possibility that antibodies to PsaA may protect against carriage of *S. pneumoniae*.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 13 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:395033 BIOSIS

DOCUMENT NUMBER: PREV200000395033

TITLE: Immunogenicity of the pneumococcal antigens PsaA and pneumolysin expressed in *S. typhi* vaccine strain CVD 908htrA.

AUTHOR(S): Barry, E. M. (1); Ruiz, F. (1); Paton, J. C.; Ades, E. W.; Sampson, J.; Carlone, G.; Levine, M. M. (1)

CORPORATE SOURCE: (1) University of Maryland, Baltimore, MD USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2000) Vol. 100, pp. 301. print.
Meeting Info.: 100th General Meeting of the American Society for Microbiology Los Angeles, California, USA May 21-25, 2000 American Society for Microbiology . ISSN: 1060-2011.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

L32 ANSWER 14 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:2705 BIOSIS

DOCUMENT NUMBER: PREV200100002705

TITLE: Inhibition of pneumococcal (Pnc) carriage in mice by subcutaneous (SC) immunization with peptides from Pnc protein PsaA.

AUTHOR(S): Johnson, S. E. (1); Dykes, J. K. (1); Jue, D. L. (1); Sampson, J. S. (1); Carlone, G. M. (1); Ades, E. W. (1)

CORPORATE SOURCE: (1) CDC, Atlanta, GA USA
SOURCE: Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 249. print.
Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy Toronto, Ontario, Canada September 17-20, 2000

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

Searcher : Shears 308-4994

09/613092

L32 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 12
ACCESSION NUMBER: 2000:273192 HCAPLUS
DOCUMENT NUMBER: 133:295042
TITLE: Selection of an immunogenic and protective
epitope of the PsaA protein of Streptococcus
pneumoniae using a phage display library
AUTHOR(S): Srivastava, N.; Zeiler, J. L.; Smithson, S. L.;
Carlone, G. M.; Ades, E. W.;
Sampson, J. S.; Johnson, S. E.
; Kieber-Emmons, T.; Westerink, M. A. J.
CORPORATE SOURCE: Department of Medicine, Medical College of Ohio,
Toledo, OH, 43614, USA
SOURCE: Hybridoma (2000), 19(1), 23-31
CODEN: HYBRDY; ISSN: 0272-457X
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Streptococcus pneumoniae is an important pathogen that causes disease in young and elderly individuals. The currently available polysaccharide vaccines have limited efficacy in those age groups most susceptible to pneumococcal infections. This study focuses on mapping the epitopes of a surface protein of S. pneumoniae by biopanning a 15 mer phage display library using 5 different monoclonal antibodies (MAbs) against the **Pneumoccal surface adhesin A (PsaA)**. PsaA is a component of the bacterial cell wall that is highly species specific and is involved in bacterial adherence and virulence. Biopanning of the phage display library reveals three distinct epitopes on the PsaA protein. The sequence homol. of these epitopes ranges from two to six amino acids when compared to the native PsaA protein type 2. Two of these epitopes have been evaluated for their immunogenicity in mice. The peptide selected by the MAbs 8G12, 6F6, and 1B7 is referred to as the consensus peptide and is immunogenic in mice. Optimal anti-PsaA response is obsd. in mice immunized with 50 .mu.g of the consensus peptide complexed to proteosomes in 1:1 ratio. The anti-PsaA response is significantly lower than the response to the PsaA native protein. The peptide selected by monoclonal antibody 4E9 in its lipidated form is significantly protective in mice challenged with S. pneumoniae serotype 2 when compared to mice immunized with the native protein. These results show that the selected epitopes of PsaA protein are immunogenic and protective in mice. These epitopes need to be evaluated further as alternatives to currently available vaccines.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L32 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
ACCESSION NUMBER: 1999:577027 HCAPLUS
DOCUMENT NUMBER: 131:198616
TITLE: Epitope peptides immunogenic against
Streptococcus pneumoniae and their use in
vaccines
INVENTOR(S): Carlone, George M.; Ades, Edwin
W.; Sampson, Jacquelyn S.;
Tharpe, Jean A.; Zeiler, Joan Louise; Westerink,
Maria Anna Julia

Searcher : Shears 308-4994

09/613092

PATENT ASSIGNEE(S): The Government of the United States of America,
Represented by the Secretary, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945121	A1	19990910	WO 1999-US4326	19990226
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2326408	AA	19990910	CA 1999-2326408	19990226
AU 9927950	A1	19990920	AU 1999-27950	19990226
BR 9908476	A	20001205	BR 1999-8476	19990226
EP 1060249	A1	20001220	EP 1999-908543	19990226
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

PRIORITY APPLN. INFO.: US 1998-76565P P 19980302
WO 1999-US4326 W 19990226

AB Peptides are provided which immunospecifically bind to monoclonal antibodies specific for the 37-kDa pneumococcal surface adhesion A protein (PsaA) of Streptococcus pneumoniae of the invention, and that are immunogenic against Streptococcus pneumoniae infection. Also provided are vaccines comprising such immunogenic polypeptides, and methods of conferring protective immunity against Streptococcus pneumoniae infection by administering therapeutic comps. comprising the immunogenic peptides of the invention. Also provided are methods of detecting the presence of Streptococcus pneumoniae in a sample using antibodies or antigens, and methods of preventing and treating Streptococcus pneumoniae infection in a subject. In addn. a phage display method of identifying the sequence of a peptide potentially capable of eliciting protective immunity against a pathogenic microorganism is provided.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 14
ACCESSION NUMBER: 1999:511257 HCAPLUS
DOCUMENT NUMBER: 131:154473
TITLE: Streptococcus pneumoniae lipidated PsaA protein, a chimeric DNA molecule encoding it, its recombinant production, isolation and purification, and its use in a vaccine for the prevention and treatment of infection
INVENTOR(S): Ades, Edwin W.; Carlone, George M.; De Barun, K.; Sampson, Jacquelyn

Searcher : Shears 308-4994

09/613092

PATENT ASSIGNEE(S): S.; Huebner, Robert C.
SOURCE: Center for Disease Control and Prevention, USA
PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940200	A1	19990812	WO 1999-US379	19990114
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319404	AA	19990812	CA 1999-2319404	19990114
AU 9923131	A1	19990823	AU 1999-23131	19990114
EP 1053329	A1	20001122	EP 1999-903011	19990114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9909097	A	20001205	BR 1999-9097	19990114
JP 2002505083	T2	20020219	JP 2000-530614	19990114
PRIORITY APPLN. INFO.:			US 1998-17782	A 19980203
			WO 1999-US379	W 19990114

AB The invention provides a chimeric DNA mol. contg. the first 52 amino acids of *Borrelia burgdorferi* gene ospA lipoprotein (including the signal peptide) fused to the mature form of *Streptococcus pneumoniae* gene **psaA pneumococcal** surface protein A (**PsaA**, previously known as **pneumococcal** fimbrial protein A). The invention also provides an expression vector contg. the chimeric DNA mol., and the use of the vector for recombinant prodn. of lipidated PsaA proteins. The invention further provides purifn. methods used to obtain the recombinant PsaA proteins, and use of these proteins in immunol. compns. Also provided are vaccines comprising immunogenic lipidated PsaA proteins and methods of use of such vaccines in the prevention and treatment of *S. pneumoniae* infection. The sequence of the chimeric DNA mol. used in the recombinant prodn. of lipidated PsaA proteins was included in the invention.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 18 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:340705 BIOSIS
DOCUMENT NUMBER: PREV199900340705
TITLE: Physicochemical analysis of *Escherichia coli*-expressed recombinant **pneumococcal surface adhesin A (rPsaA)** of *Streptococcus pneumoniae* by mass spectrometry.
AUTHOR(S): De, B. (1); Sampson, J. S.; Ades, E. W.; Huebner, R. C.; Jue, D. L.;

Searcher : Shears 308-4994

Wohlhueter, R. M.; **Carlone, G. M.**
 CORPORATE SOURCE: (1) Pasteur Merieux Connaught Labs., Atlanta, GA USA
 SOURCE: Abstracts of the General Meeting of the American
 Society for Microbiology, (1999) Vol. 99, pp. 369.
 Meeting Info.: 99th General Meeting of the American
 Society for Microbiology Chicago, Illinois, USA May
 30-June 3, 1999 American Society for Microbiology
 . ISSN: 1060-2011.
 DOCUMENT TYPE: Conference
 LANGUAGE: English

L32 ANSWER 19 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1999:325963 BIOSIS
 DOCUMENT NUMBER: PREV199900325963
 TITLE: Expression of PsaA from Streptococcus pneumoniae in
 S. typhi vaccine strain CVD 908htrA.
 AUTHOR(S): Barry, E. M. (1); Ruiz, F. (1); **Sampson, J.**
S.; Ades, E. W.; Carlone, G.
M.; Levine, M. M. (1)
 CORPORATE SOURCE: (1) University of Maryland, Baltimore, MD USA
 SOURCE: Abstracts of the General Meeting of the American
 Society for Microbiology, (1999) Vol. 99, pp. 293.
 Meeting Info.: 99th General Meeting of the American
 Society for Microbiology Chicago, Illinois, USA May
 30-June 3, 1999 American Society for Microbiology
 . ISSN: 1060-2011.
 DOCUMENT TYPE: Conference
 LANGUAGE: English

L32 ANSWER 20 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1999:325906 BIOSIS
 DOCUMENT NUMBER: PREV199900325906
 TITLE: Immunologic characterization of a monoclonal antibody
 to Streptococcus pneumoniae **pneumococcal**
surface adhesin A (PsaA)
 protein.
 AUTHOR(S): **Sampson, J. S. (1); Ades, E. W. (1)**
 ; Romero-Steiner, S. (1); **Johnson, S. (1);**
 Daugharty, H. (1); Dykes, J. (1); Stinson, A. (1);
 Crook, J. (1); **Carlone, G. M. (1)**
 CORPORATE SOURCE: (1) CDC, Atlanta, GA USA
 SOURCE: Abstracts of the General Meeting of the American
 Society for Microbiology, (1999) Vol. 99, pp. 273.
 Meeting Info.: 99th General Meeting of the American
 Society for Microbiology Chicago, Illinois, USA May
 30-June 3, 1999 American Society for Microbiology
 . ISSN: 1060-2011.
 DOCUMENT TYPE: Conference
 LANGUAGE: English

L32 ANSWER 21 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1999:399813 BIOSIS
 DOCUMENT NUMBER: PREV199900399813
 TITLE: Antibodies to **pneumococcal** proteins
PsaA, PspA and pneumoclysin in saliva of
 children.
 AUTHOR(S): Stenroos, B. (1); Korkeila, M. (1); Syrianeni, R.
 (1); Briles, D.; Becker, R.; **Carlone, G.;**

09/613092

CORPORATE SOURCE: Sampson, J.; Paton, I.; Kilpii, T. (1);
Takalai, A. (1); Kayhtyt, H. (1)
SOURCE: (1) KTL, Helsinki Finland
Immunology Letters, (June 15, 1999) Vol. 69, No. 1,
pp. 139.
Meeting Info.: 10th International Congress of Mucosal
Immunology Amsterdam, Netherlands June 27-July 1, 1999
ISSN: 0165-2478.
DOCUMENT TYPE: Conference
LANGUAGE: English

L32 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 15

ACCESSION NUMBER: 1999:436611 HCAPLUS

DOCUMENT NUMBER: 131:86646

TITLE: Baculovirus expression, purification, and
evaluation of recombinant **pneumococcal**
surface adhesin A of
Streptococcus pneumoniae

AUTHOR(S): De, B. K.; Sampson, J. S.; Ades,
E. W.; Johnson, S. E.; Stinson,
A. R.; Crook, J.; Tharpe, J. A.; Huebner, R. C.;
Carlone, G. M.

CORPORATE SOURCE: Division Bacterial Mycotic Diseases, Centers
Disease Control Prevention, National Center
Infectious Diseases, Atlanta, GA, 30333, USA

SOURCE: Pathobiology (1999), 67(3), 115-122

CODEN: PATHEF; ISSN: 1015-2008

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Pneumococcal surface adhesin A** (**PsaA**), with a mol. mass of 37 kD by SDS-PAGE, is a common surface protein expressed by all 90 serotypes of *S. pneumoniae*. *S. pneumoniae* serotype 6B genomic DNA was amplified to generate a DNA fragment carrying the full-length *psaA* sequence and was cloned into a baculovirus expression system. The authors expressed either cell-assocd. or cell-free nonfusion PsaA polypeptides using 2 insect cell lines, *Spodoptera frugiperda* (Sf9) and *Trichoplusia ni* 5B1-4 (High-Five). Recombinant PsaA (rPsaA) polypeptides were partially purified by partitioning in PBS/Triton X-114 buffers and by weakly basic ion exchange filter chromatog. Membrane-bound "hydrophobic rPsaA" (hrPsaA) expressed by either Sf9 or High-Five cells had a mol. mass of 38 kD by SDS-PAGE and partitioned in a Triton X-114 phase, it reacted with both rabbit polyclonal and 5 monoclonal anti-PsaA antibodies by dot blot or Western blot. High-Five-cell-expressed "sol. rPsaA" (srPsaA) with a mol. mass of 37 kD by SDS-PAGE, was isolated from the serum-free culture medium and did not partition in the Triton X-114 phase; it reacted with anti-PsaA rabbit polyclonal and mouse monoclonal antibodies by ELISA and Western blot. Both rPsaA polypeptide forms were immunogenic in adult mice. In an infant mouse model of bacteremia, survival rates for mice given mouse anti-rPsaA immune serum (from mice immunized with High-Five-expressed srPsaA; 20 μ l, 1:50,000 titer) 24 h before bacteremic challenge were greater than for the control group (48 h post-challenge, 20 vs. 90% survival rates) when challenged with *S. pneumoniae* serotype 6B. These results indicate that rPsaA is immunogenic and elicits protective antibody in mice similar to native protein.

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REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L32 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 16
ACCESSION NUMBER: 1999:21723 HCAPLUS
DOCUMENT NUMBER: 130:77112
TITLE: Streptococcus pneumoniae 37-
kDa surface adhesin A protein and its
gene
INVENTOR(S): Sampson, Jacquelyn S.; Russell,
Harold; Tharpe, Jean A.; Ades, Edwin W.
; Carlone, George M.
PATENT ASSIGNEE(S): United States Dept. of Health and Human
Services, USA
SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No.
222,179, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5854416	A	19981229	US 1996-715131	19960917
US 5422427	A	19950606	US 1991-791377	19911114
US 6312944	B1	20011106	US 1994-356106	19941215
US 6217884	B1	20010417	US 1998-221753	19981228
PRIORITY APPLN. INFO.:			US 1991-791377	A2 19911114
			US 1994-222179	B2 19940404
			US 1996-715131	A3 19960917

AB The invention provides a nucleic acid encoding the 37-
kDa protein from Streptococcus pneumoniae. Also
provided are isolated nucleic acids comprising a unique fragment of
at least 10 nucleotides of the 37-kDa protein. The invention also
provides purified polypeptides encoded by the nucleic acid encoding
the 37-kDa protein from and the nucleic acids comprising a unique
fragment of at least 10 nucleotides of the 37-kDa protein. Also
provided are antibodies which selectively binds the polypeptides
encoded by the nucleic acid encoding the 37-kDa protein and the
nucleic acids comprising a unique fragment of at least 10
nucleotides of the 37-kDa protein. Also provided are vaccines
comprising immunogenic polypeptides encoded by the nucleic acid
encoding the 37-kDa protein and the nucleic acids comprising a
unique fragment of at least 10 nucleotides of the 37-kDa protein.
Further provided is a method of detecting the presence of
Streptococcus pneumoniae in a sample comprising the steps of
contacting a sample suspected of contg. Streptococcus pneumoniae
with nucleic acid primers capable of hybridizing to a nucleic acid
comprising a portion of the nucleic acid encoding the 37-kDa
protein, amplifying the nucleic acid and detecting the presence of
an amplification product, the presence of the amplification product
indicating the presence of Streptococcus pneumoniae in the sample.
Further provided are methods of detecting the presence of
Streptococcus pneumoniae in a sample using antibodies or antigens,
methods of preventing and treating Streptococcus pneumoniae
infection in a subject.

Searcher : Shears 308-4994

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REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L32 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 17
ACCESSION NUMBER: 1998:234181 HCAPLUS
DOCUMENT NUMBER: 128:307320
TITLE: Immunoreactivity of five monoclonal antibodies
against the **37-kilodalton**
common cell wall protein (PsaA) of *Streptococcus*
pneumoniae
AUTHOR(S): Crook, Jennifer; Tharpe, Jean A.; Johnson,
Scott E.; Williams, Derrick B.; Stinson,
Annie R.; Facklam, Richard R.; **Ades, Edwin**
W.; **Carlone, George M.**;
Sampson, Jacquelyn S.
CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases,
National Center for Infectious Diseases, Centers
for Disease Control and Prevention, U.S.
Department of Health and Human Services,
Atlanta, GA, 30333, USA
SOURCE: Clinical and Diagnostic Laboratory Immunology
(1998), 5(2), 205-210
CODEN: CDIMEN; ISSN: 1071-412X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Five monoclonal antibodies (MAbs) were produced against the
Streptococcus pneumoniae **pneumococcal**
surface adhesin A (PsaA) 37-
kDa common cell wall protein. These antibodies were used in
a dot immunoblot and Western blot study of clin. isolates of *S.*
pneumoniae to detect the presence of the protein. By both assays,
the MAbs reacted with clin. isolates representing the 23
type-specific serotypes present in the licensed pneumococcal
polysaccharide vaccine. Western blot anal. confirmed the presence
of a protein migrating in the gel with a mol. mass of 37 kDa. An
extension of the study by using dot immunoblot anal. that included
an anal. of the 90 serotypes of *S. pneumoniae* showed that all five
MAbs reacted with 89 of the 90 serotypes tested. MAb 1B6, the
exception, did not react with *S. pneumoniae* serotype 16F. Dot
immunoblot anal. of the MAbs with *Enterococcus faecalis* and *viridans*
streptococci showed varied reactivity patterns, depending on the
species. The MAbs against the 37-kDa antigen did not react with
Escherichia coli, respiratory pathogens, or nonpathogens
representing 22 genera and 29 species of bacteria. All five MAbs
also reacted with five multidrug-resistant strains of *S. pneumoniae*.
In summary, these MAbs may be useful for detection of pneumococcal
antigen and may lead to the development of diagnostic assays for
pneumococcal disease.

L32 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 18
ACCESSION NUMBER: 1998:325125 HCAPLUS
DOCUMENT NUMBER: 128:319014
TITLE: Comparison of a **pneumococcal** common
protein (**PsaA**) antibody ELISA and a
PsaA immune complex ELISA for detection
of **pneumococcal** serum antibody

Searcher : Shears 308-4994

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AUTHOR(S): Tharpe, Jean A.; Russell, Harold; Leinonen, Maija; Plikaytis, Brian D.; Breiman, Robert F.; Carlone, George M.; Ades, Edwin A.; Sampson, Jacquelyn S.

CORPORATE SOURCE: Respiratory Diseases Branch, Div. Bacterial Mycotic Diseases, National Center Infectious Diseases, Centers Disease Control Prevention, Atlanta, GA, 30333, USA

SOURCE: Pathobiology (1998), 66(2), 77-83
CODEN: PATHEF; ISSN: 1015-2008

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors examd. and compared results from 3 assays, an ELISA and 2 immune complex ELISAs for anal. of the blood serum antibody response to a native pneumococcal 37-kD common cell-wall protein by acute- and convalescent-phase sera from patients with community-acquired pneumonia. The sensitivities of the ELISA, the undissociated and dissocd. immune complex assays were 85, 78, and 67% (23, 21, and 18 of 27), resp. To det. specificity, paired sera from patients with pneumonia of other bacterial etiologies were tested. The specificities were 83, 83, and 72% for the ELISA, undissociated immune complex, and dissocd. immune complex, resp. These tests were used retrospectively to confirm invasive pneumococcal disease.

L32 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 19

ACCESSION NUMBER: 1997:307005 HCAPLUS

DOCUMENT NUMBER: 127:31404

TITLE: Limited diversity of Streptococcus pneumoniae **psaA** among pneumococcal vaccine serotypes

AUTHOR(S): Sampson, Jacquelyn S.; Furlow, Zabrina; Whitney, Anne M.; Williams, Derrick; Facklam, Richard; Carlone, George M.

CORPORATE SOURCE: Division of bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, 30333, USA

SOURCE: Infection and Immunity (1997), 65(5), 1967-1971
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **pneumococcal surface adhesin A (PsaA)** is a surface-exposed protein of the gram-pos. bacterium Streptococcus pneumoniae. It belongs to a group of proteins designated the lipoprotein receptor I antigen family. The gene encoding **PsaA** from an encapsulated strain of pneumococcal serotype 6B was cloned and sequenced. The peptide sequence was compared to that of homologs found in S. pneumoniae serotype 2, viridans streptococci, and Enterococcus faecalis. Identity values among the deduced peptides ranged from 57 to 98%. The polymorphism of **psaA** was examd. among the 23 encapsulated vaccine serotypes by using PCR-restriction fragment length polymorphism anal. Ten different enzymes were used to analyze 80 strains representing the 23 serotypes in a 23-valent polysaccharide vaccine. This anal. showed that restriction sites

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within the gene were highly conserved, with only a minor variation occurring in 10% of the strains, the result of an addnl. Tsp5091 site. The lack of variation for the other restriction sites within the gene examd. here indicates that psaA is genetically conserved, an important characteristic necessary for a candidate common protein vaccine.

L32 ANSWER 27 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:284892 BIOSIS
DOCUMENT NUMBER: PREV199799584095
TITLE: Native and recombinant Streptococcus pneumoniae
PsaA: Comparison of antibodies in pneumococcal pneumonia patient sera by ELISA.
AUTHOR(S): Espina, M. L. (1); Tharpe, J. A.; Crook, J.; Stinson, A. R.; Paton, J. A.; **Ades, E. W.; Carlone, G. M.; Sampson, J. S.**
CORPORATE SOURCE: (1) Cent. Disease Control and Prevention, Atlanta, GA USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1997) Vol. 97, No. 0, pp. 576.
Meeting Info.: 97th General Meeting of the American Society for Microbiology Miami Beach, Florida, USA May 4-8, 1997
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; Abstract; Conference
LANGUAGE: English

L32 ANSWER 28 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:283001 BIOSIS
DOCUMENT NUMBER: PREV199799582204
TITLE: Baculovirus expressed recombinant
pneumococcal surface adhesin A (rPsaA) of Streptococcus pneumoniae serotype 6B generates murine antibodies capable of passive protection in an infant mouse model of bacteremia.
AUTHOR(S): De, B. K. (1); **Johnson, S. E.; Ades, E. W.; Stinson, A. R.; Crook, J.; Huebner, R. C. (1); Sampson, J. S.; Carlone, G. M.**
CORPORATE SOURCE: (1) Connaught Lab. Inc., Swiftwater, PA USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1997) Vol. 97, No. 0, pp. 251.
Meeting Info.: 97th General Meeting of the American Society for Microbiology Miami Beach, Florida, USA May 4-8, 1997
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L32 ANSWER 29 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:282984 BIOSIS
DOCUMENT NUMBER: PREV199799582187
TITLE: Epitope mapping of a species-specific 37-kDa lipoprotein present in all Streptococcus pneumoniae capsular serotypes.
pneumoniae capsular serotypes.
AUTHOR(S): Zeiler, J. L.; **Sampson, J. S.;**

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CORPORATE SOURCE: **Carlone, G. M.; Ades, E. W.;**
SOURCE: **Westerink, M. A. J.**
Med. College Ohio, Toledo, OH USA
Abstracts of the General Meeting of the American
Society for Microbiology, (1997) Vol. 97, No. 0, pp.
248.
Meeting Info.: 97th General Meeting of the American
Society for Microbiology Miami Beach, Florida, USA
May 4-8, 1997
ISSN: 1060-2011.
DOCUMENT TYPE: **Conference; Abstract; Conference**
LANGUAGE: **English**

L32 ANSWER 30 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:282905 BIOSIS
DOCUMENT NUMBER: PREV199799582108
TITLE: **Immunoreactivity of five monoclonal antibodies**
against the 37-kilodalton common
cell-wall protein of Streptococcus pneumoniae

AUTHOR(S): **Crook, J.; Tharpe, J.; Johnson, S.;**
Williams, D.; Stinson, A.; Carlone, G.;
Ades, E.; Sampson, J.
CORPORATE SOURCE: **Cent. Disease Control Prevention, Atlanta, GA USA**
SOURCE: **Abstracts of the General Meeting of the American**
Society for Microbiology, (1997) Vol. 97, No. 0, pp.
234.
Meeting Info.: 97th General Meeting of the American
Society for Microbiology Miami Beach, Florida, USA
May 4-8, 1997
ISSN: 1060-2011.
DOCUMENT TYPE: **Conference; Abstract; Conference**
LANGUAGE: **English**

L32 ANSWER 31 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:525960 BIOSIS
DOCUMENT NUMBER: PREV199598540260
TITLE: **Conservation of the 37-kDa**
protein gene among Streptococcus pneumoniae
serotypes.

AUTHOR(S): **Sampson, J.; Furlow, Z.; Williams, D.**
CORPORATE SOURCE: **Centers for Disease Control and Prevention, Atlanta,**
GA 30333 USA
SOURCE: **Abstracts of the Interscience Conference on**
Antimicrobial Agents and Chemotherapy, (1995) Vol.
35, No. 0, pp. 164.
Meeting Info.: 35th Interscience Conference on
Antimicrobial Agents and Chemotherapy San Francisco,
California, USA September 17-20, 1995
DOCUMENT TYPE: **Conference**
LANGUAGE: **English**

L32 ANSWER 32 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:525479 BIOSIS
DOCUMENT NUMBER: PREV199598539779
TITLE: **Detection and evaluation of circulating immune**
complexes containing antibodies to a pneumococcal
37-kDa common protein in

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pneumococcal **pneumonia** patients.
AUTHOR(S): Tharpe, J. A.; Russell, H.; **Sampson, J. S.**
CORPORATE SOURCE: Centers Diseases Control Prevention, Atlanta, GA
30333 USA
SOURCE: Abstracts of the Interscience Conference on
Antimicrobial Agents and Chemotherapy, (1995) Vol.
35, No. 0, pp. 78.
Meeting Info.: 35th Interscience Conference on
Antimicrobial Agents and Chemotherapy San Francisco,
California, USA September 17-20, 1995
DOCUMENT TYPE: Conference
LANGUAGE: English

L32 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 20
ACCESSION NUMBER: 1994:126489 HCAPLUS
DOCUMENT NUMBER: 120:126489
TITLE: Cloning and nucleotide sequence analysis of
psaA, the Streptococcus **pneumoniae**
gene encoding a 37-kilodalton
protein homologous to previously reported
Streptococcus sp. adhesins
AUTHOR(S): **Sampson, Jacquelyn S.**; O'Connor,
Steven P.; Stinson, Annie R.; Tharpe, Jeane A.;
Russell, Harold
CORPORATE SOURCE: Div. Bac. Mycotic Dis., Natl. Cent. Infect.
Dis., Atlanta, GA, 30333, USA
SOURCE: Infect. Immun. (1994), 62(1), 319-24
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Gene psaA, which encodes the Streptococcus **pneumoniae**,
37-kDa protein, was cloned in Escherichia coli,
and its complete nucleotide sequence was detd. Anal. of the
sequence of the 2.4-kb cloned fragment revealed three open reading
frames (ORFs). ORF2, which is 933 bp long, was identified as psaA.
The two other ORFs identified flank psaA. ORF1, located upstream of
psaA, is 836 nucleotides long and encodes a protein with a calcd.
mol. mass of 29,843 Da. The sequence of ORF3, located downstream of
psaA, was only partially detd. Northern (RNA) blot anal. of
pneumococcal RNA suggests that **psaA** is transcribed
as part of a polycistronic message. Anal. of the primary structure
of the protein encoded by this gene indicated significant similarity
to two previously reported streptococcal proteins, SsaB (80%
similarity) and FimA (92.3% similarity), from S. sanguis and S.
parasanguis, resp. These two homologous proteins have been shown to
be assocd. with bacterial adhesion, and the possibility of a similar
role for PsaA is hypothesized.

L32 ANSWER 34 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1991:381249 BIOSIS
DOCUMENT NUMBER: BR41:53639
TITLE: MOLECULAR CLONING OF THE GENE ENCODING THE 37
-KILODALTON PROTEIN OF STREPTOCOCCUS-
PNEUMONIAE.
AUTHOR(S): **SAMPSON J**; O'CONNOR S; STINSON A; THARPE J;
RUSSELL H
CORPORATE SOURCE: CENT. DIS. CONTROL, ATLANTA, GA., USA.
SOURCE: 91ST GENERAL MEETING OF THE AMERICAN SOCIETY FOR

Searcher : Shears 308-4994

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MICROBIOLOGY 1991, DALLAS, TEXAS, USA, MAY 5-9, 1991.
ABSTR GEN MEET AM SOC MICROBIOL, (1991) 91 (0), 97.
CODEN: AGMME8.

DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

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Alert feature enhanced for multiple files, etc. See HELP ALERT.
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Set	Items	Description
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S1	98	PSAA(10N)PNEUMOC? OR PNEUMOC?(W)SURFACE(W) (ANTIGEN? ? OR A-DHES?) OR PNEUMON?(10N) (37KD? OR 37KILOD? OR 37(W) (KD? OR KIL-OD? OR KILO(W) (D OR DALTON? ? OR DA)))
S2	20	S1 AND (MOAB? ? OR MAB? ? OR MONOCLON? OR 4E9 OR 1B6 OR 8G-12 OR 6F6 OR 1E7)
S3	12	RD (unique items)

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-key terms

3/3,AB/1 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online
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01653353 AAD1390146

MAPPING OF IMMUNOGENIC EPITOPES COMMON TO ALL STREPTOCOCCUS PNEUMONIAE
SEROTYPES

Author: ZEILER, JOAN LOUISE
Degree: M.S.
Year: 1998
Corporate Source/Institution: MEDICAL COLLEGE OF OHIO AT TOLEDO (0539)
Source: VOLUME 36/06 of MASTERS ABSTRACTS.
PAGE 1578. 81 PAGES

Streptococcus pneumoniae causes morbidity and mortality throughout the world today. The present vaccine is a 23-valent PS vaccine, not effective in neonates and elderly due to the T-cell independent nature of the vaccine. Efforts are being sought to design a pneumococcal vaccine that provides protection in all age groups. A conserved *pneumococcal*** protein, species-common 37-kilodalton lipoprotein (*PsaA***), is being evaluated as a possible vaccine candidate. *Monoclonal*** antibodies (*mAbs***) made with specificity to the *PsaA*** protein are cross-reactive

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among all tested *pneumococcus*** species. Passive immunization studies with *PsaA*** specific *mAbs*** have shown to be protective against challenge. These five *mAbs*** were used as tools to screen a peptide library to determine the immunogenic epitopes found on the PsaA protein. A peptide was determined and synthesized through analysis of the amino acid sequences. Future studies will be directed towards the evaluation of the conserved peptide as a logical vaccine candidate.

3/3,AB/2 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
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15537815 PASCAL No.: 02-0236326

Inhibition of pneumococcal carriage in mice by subcutaneous immunization with peptides from the common surface protein *pneumococcal*** *surface*** *adhesin*** A

JOHNSON Scott E; DYKES Janet K; JUE Danny L; SAMPSON Jaquelyn S; CARLONE George M; ADES Edwin W

Division of Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, United States; Scientific Resources Program, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, United States

Journal: The Journal of infectious diseases, 2002, 185 (4) 489-496

Language: English

*Pneumococcal*** *surface*** *adhesin*** A (*PsaA***), a common protein expressed on all 90 *pneumococcal*** serotypes, is a vaccine candidate. Three anti-*PsaA*** *monoclonal*** antibody phage display-expressed mono-peptides (15 mers), in various formulations as lipidated or nonlipidated multiantigenic peptides or as bi- or tripeptide constructs, were studied in a mouse nasopharyngeal carriage model to determine the inhibitory effect of induced antibodies on carriage of pneumococcal serotypes 2, 4, and 6B. Antibodies to each of the various peptides tested reduced carriage of the 3 serotypes. Reduction in carriage by nonlipidated multiantigenic peptide antibodies was highly variable (39%-94%; mean, 59%; standard deviation (SD), 20.2%); however, more-consistent results were observed in mice immunized with lipidated (56%-98%; mean, 69%; SD, 13.6%) and combination or bi-peptide (55%-91%; mean, 76%; SD, 13.1%) formulations. These peptides are immunogenic, and their induced antibodies reduce carriage in mice. *PsaA*** peptides demonstrate potential for being important new vaccines against *pneumococcal*** carriage, otitis media, and invasive pneumococcal disease.

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3/3,AB/3 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal
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14552099 PASCAL No.: 00-0217784

Selection of an immunogenic and protective epitope of the PsaA protein of Streptococcus pneumoniae using a phage display library

SRIVASTAVA N; ZEILER J L; SMITHSON S L; CARLONE G M; ADES E W; SAMPSON J S; JOHNSON S E; KIEBER-EMMONS T; WESTERINK M A J

Department of Medicine, Medical College of Ohio, Toledo, OH 43614, United States; Department of Pathology, Medical College of Ohio, Toledo, OH 43614, United States; Division of Bacterial and Mycotic Diseases, National Center

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for Infectious Diseases, Centers for Disease Control and Prevention.,
Atlanta, GA 30333, United States; Department of Pathology and Lab Medicine,
University of Pennsylvania., Philadelphia, PA 19104, United States

Journal: Hybridoma, 2000, 19 (1) 23-31

Language: English

Streptococcus pneumoniae is an important pathogen that causes disease in young and elderly individuals. The currently available polysaccharide vaccines have limited efficacy in those age groups most susceptible to pneumococcal infections. This study focuses on mapping the epitopes of a surface protein of *S. pneumoniae* by biopanning a 15 mer phage display library using 5 different *monoclonal*** antibodies (*MAbs***). *PsaA*** is a component of the bacterial cell wall that is highly species specific and is involved in bacterial adherence and virulence. Biopanning of the phage display library reveals three distinct epitopes on the PsaA protein. The sequence homology of these epitopes ranges from two to six amino acids when compared to the native PsaA protein type 2. Two of these epitopes have been evaluated for their immunogenicity in mice. The peptide selected by the *MAbs*** *8G12***, *6F6***, and 1B7 is referred to as the consensus peptide and is immunogenic in mice. Optimal anti-PsaA response is observed in mice immunized with 50 mu g of the consensus peptide complexed to proteosomes in 1:1 ratio. The anti-PsaA response is significantly lower than the response to the PsaA native protein. The peptide selected by *monoclonal*** antibody *4E9*** in its lipidated form is significantly protective in mice challenged with *S. pneumoniae* serotype 2 when compared to mice immunized with the native protein. These results show that the selected epitopes of PsaA protein are immunogenic and protective in mice. These epitopes need to be evaluated further as alternatives to currently available vaccines.

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3/3,AB/4 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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10747269 References: 38

TITLE: Baculovirus expression, purification and evaluation of recombinant
*pneumococcal*** *surface*** *adhesin*** A of *Streptococcus pneumoniae*

AUTHOR(S): De BK (REPRINT); Sampson JS; Ades EW; Johnson SE; Stinson AR;
Crook J; Tharpe JA; Huebner RC; Carlone GM

AUTHOR(S) E-MAIL: bkd1@cdc.gov

CORPORATE SOURCE: Ctr Dis Control & Prevent, Div Bacterial & Mycot Dis, MS
G05,1600 Clifton Rd NE/Atlanta//GA/30333 (REPRINT); Ctr Dis Control &
Prevent, Div Bacterial & Mycot Dis, /Atlanta//GA/30333; Pasteur Merieux
Connaught Labs Inc, /Swiftwater//PA/

PUBLICATION TYPE: JOURNAL

PUBLICATION: PATHOBIOLOGY, 1999, V67, N3 (MAY-JUN), P115-122

GENUINE ARTICLE#: 214QF

PUBLISHER: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND

ISSN: 1015-2008

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: *Pneumococcal*** *surface*** *adhesin*** A (*PsaA***), with a molecular mass of similar to 37 kD by SDS-PAGE, is a common surface protein expressed by all 90 serotypes of *Streptococcus pneumoniae*. *S. pneumoniae* serotype 6B genomic DNA was amplified to generate a DNA fragment carrying the full-length psaA sequence and was cloned into a baculovirus expression

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system. We expressed either cell-associated or cell-free nonfusion PsaA polypeptides using two insect cell lines, *Spodoptera frugiperda* (Sf9) and *Trichoplusia ni* 5B1-4 (High-Five). Recombinant PsaA (rPsaA) polypeptides were partially purified by partitioning in PBS/Triton X-114 buffers and by weakly basic ion exchange filter chromatography. Membrane-bound 'hydrophobic rPsaA' (hrPsaA) expressed by either Sf9 or High-Five cells had a molecular mass of similar to 38 kD by SDS-PAGE and partitioned in a Triton X-114 phase, it reacted with both rabbit polyclonal and five *monoclonal*** anti-PsaA antibodies by dot blot or Western blot analysis.

3/3,AB/5 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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09277342 References: 50

TITLE: Immunoreactivity of five *monoclonal*** antibodies against the
*37***-kilodalton*** common cell wall protein (PsaA) of *Streptococcus*
*pneumoniae***

AUTHOR(S): Crook J; Tharpe JA; Johnson SE; Willlams DB; Stinson AR; Facklam
RR; Ades EW; Carlone GM; Sampson JS (REPRINT)

CORPORATE SOURCE: CTR DIS CONTROL & PREVENT, DIV BACTERIAL & MYCOT DIS, NATL
CTR INFECT DIS, US DEPT HHS/ATLANTA//GA/30333 (REPRINT); CTR DIS CONTROL
& PREVENT, DIV BACTERIAL & MYCOT DIS, NATL CTR INFECT DIS, US DEPT
HHS/ATLANTA//GA/30333

PUBLICATION TYPE: JOURNAL

PUBLICATION: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, 1998, V5, N2 (MAR), P205-210

GENUINE ARTICLE#: ZA823

PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW,
WASHINGTON, DC 20005-4171

ISSN: 1071-412X

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Five *monoclonal*** antibodies (*MAbs***) were produced against the *Streptococcus* *pneumoniae*** *pneumococcal*** *surface*** *adhesin*** A (*PsaA***) *37***-kDa*** common cell wall protein. These antibodies were used in a dot immunoblot and Western blot study of clinical isolates of *S. pneumoniae* to detect the presence of the protein. By both assays, the *MAbs*** reacted with clinical isolates representing the 23 type-specific serotypes present in the licensed pneumococcal polysaccharide vaccine. Western blot analysis confirmed the presence of a protein migrating in the gel with a molecular mass of 37 kDa. An extension of the study by using dot immunoblot analysis that included an analysis of the 90 serotypes of *S. pneumoniae* showed that all five *MAbs*** reacted with 89 of the 90 serotypes tested. *MAB*** *1B6***, the exception, did not react with *S. pneumoniae* serotype 16F. Dot immunoblot analysis of the *MAbs*** with *Enterococcus faecalis* and viridans streptococci showed varied reactivity patterns, depending on the species. The *MAbs*** against the 37-kDa antigen did not react with *Escherichia coli*, respiratory pathogens, or nonpathogens representing 22 genera and 29 species of bacteria. All five *MAbs*** also reacted with five multidrug-resistant strains of *S. pneumoniae*. In summary, these *MAbs*** may be useful for detection of pneumococcal antigen and may lead to the development of diagnostic assays for pneumococcal disease.

3/3,AB/6 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

09/613092

(c) 2002 Inst for Sci Info. All rts. reserv.

08614007 References: 131

TITLE: Immunologic epitope, gene, and immunity involved in pneumococcal glycoconjugate

AUTHOR(S): Lee CJ (REPRINT); Wang TR; Tai SS

CORPORATE SOURCE: US FDA,CTR BIOL EVALUAT & RES/ROCKVILLE//MD/20852

(REPRINT); HOWARD UNIV,COLL MED, DEPT MICROBIOL/WASHINGTON//DC/20059

PUBLICATION TYPE: JOURNAL

PUBLICATION: CRITICAL REVIEWS IN MICROBIOLOGY, 1997, V23, N2, P121-142

GENUINE ARTICLE#: XJ351

PUBLISHER: CRC PRESS INC, 2000 CORPORATE BLVD NW, JOURNALS CUSTOMER

SERVICE, BOCA RATON, FL 33431

ISSN: 1040-841X

LANGUAGE: English DOCUMENT TYPE: REVIEW

ABSTRACT: Pneumococcal infection persists as a major cause of pneumonia, otitis media, and meningitis in infants. Children less than 2 years of age show the highest incidence of pneumococcal diseases. Production of *monoclonal*** antibody (*Mab***) to polysaccharide (PS) and binding characteristics to PS epitopes were studied. Removal of the O-acetyl group from 9V PS by alkali hydrolysis resulted in a decreased binding with rabbit 9V antiserum (AS). However, the binding reaction with 9V *Mab*** was less affected by the loss of O-acetyl content. Type 9V IgG *Mab*** provided passive protection and enhanced the opsonophagocytic activity of polymorphonuclear (PMN) leukocytes to kill type 9V pneumococci.

The pathogenecity of pneumococci is attributed to various virulence factors distributed on the cell surface, including capsular polysaccharide and protein antigens, for example, pneumolysin, autolysin, *pneumococcal*** surface protein A (PspA), *pneumococcal*** *surface*** *adhesion*** (*PsaA***), and hemin binding protein. Some of these protein antigens may be used as a component to combine with pneumococcal PS vaccine or as a carrier of conjugate vaccine.

Clinical trials of pneumococcal conjugate vaccines showed that covalent linkage of capsular PS to protein carriers improved the immunogenicity of the PS. Development of glycoconjugate vaccine for selected pneumococcal types will help solve the problem of poor immunogenicity of PS vaccine in young children used for prevention of pneumococcal infection.

3/3,AB/7 (Item 1 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

(c) 2002 European Patent Office. All rts. reserv.

00634124

Novel plasmid for production of CRM protein and diphtheria toxin.

Neues Plasmid zur Herstellung von CRM-Protein und Diphtherie-Toxin.

Nouveau plasmide pour la production de la proteine CRM et de la toxine de la diphtherie.

PATENT ASSIGNEE:

AMERICAN CYANAMID COMPANY, (212592), One Cyanamid Plaza, Wayne New Jersey

07470, (US), (applicant designated states:

AT;BE;CH;DE;DK;ES;FR;GB;GR;IE;IT;LI;LU;NL;PT;SE)

INVENTOR:

Metcalf, Benjamin J., 2480 Elmwood Avenue, Rochester, New York 14618,

(US)

Searcher : Shears 308-4994

09/613092

LEGAL REPRESENTATIVE:

Wachtershauser, Gunter, Prof. Dr. (12711), Patentanwalt Tal 29, D-80331
Munchen, (DE)

PATENT (CC, No, Kind, Date): EP 616034 A2 940921 (Basic)
EP 616034 A3 961016

APPLICATION (CC, No, Date): EP 94101770 940207;

PRIORITY (CC, No, Date): US 27283 930305

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL;
PT; SE

INTERNATIONAL PATENT CLASS: C12N-015/77; C12N-015/87; C12N-015/31;
C12N-001/21; C12N-001/21; C12R-001/16

ABSTRACT EP 616034 A3

The invention pertains to a novel method and plasmid system for producing abundant quantities of CRM197 protein, diphtheria toxin or other CRM proteins related to diphtheria toxin, as well as to microorganisms transformed with the novel plasmid. A particularly preferred DNA plasmid, designated pPX 3511, that combines the gene for CRM197 from the nontoxigenic betaphage and the plasmid pNG2-22 is described. The novel plasmid system is capable of transforming strains of Corynebacterium diphtheriae into strains which are capable of expressing high levels of the CRM197 protein without the use of multiple lysogens. The invention provides in elegant means for increasing protein production without having to manipulate the expression vector, such as by increasing the promoter strength, or removing the promoter from iron regulation. (see image in original document)

ABSTRACT WORD COUNT: 150

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF2	222
SPEC A	(English)	EPABF2	3485
Total word count - document A			3707
Total word count - document B			0
Total word count - documents A + B			3707

3/3,AB/8 (Item 1 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

(c) 2002 Thomson Derwent & ISI. All rts. reserv.

0243753 DBA Accession No.: 1999-14518 PATENT

New peptides corresponding to Streptococcus pneumoniae PsaA, used for treating or preventing Streptococcus pneumoniae infection in a subject - phage FUSE-5-mediated gene transfer and expression in Escherichia coli to create a phage DNA library

AUTHOR: Carlone G M; Ades E W; Sampson J S; Tharpe J A; Zeiler J L; Westerink M A J

CORPORATE SOURCE: Atlanta, GA, USA.

PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 1999

PATENT NUMBER: WO 9945121 PATENT DATE: 19990910 WPI ACCESSION NO.:
1999-540849 (1945)

PRIORITY APPLIC. NO.: US 76565 APPLIC. DATE: 19980302

NATIONAL APPLIC. NO.: WO 99US4326 APPLIC. DATE: 19990226

LANGUAGE: English

ABSTRACT: Peptides that immunospecifically bind to a *monoclonal***
antibody (*Mab***) obtained in response to immunizing an animal with

09/613092

Streptococcus pneumoniae (SP) *pneumococcal*** *surface*** *adhesion***
-A protein (*PsaA***) are new. Also claimed are: a peptide produced by providing a library of random oligonucleotides, splicing the oligonucleotides into the gene for gene-III coat protein of a filamentous phage (e.g. phage FUSE-5) to create a phage library, expanding the phage library by culturing in a host (e.g. Escherichia coli Kq1/kan+), screwing the expanded library for a specific phage particle that immunospecifically reacts with a *MAb*** obtained in response to immunizing an animal with SP PsaA and sequencing the gene for the coat protein of the phage obtained; a therapeutic composition containing one or more peptides produced; and a peptide containing a sequence at least 80% identical to defined peptides. The peptides can be used for treating or preventing infection by SP in a subject. (58pp)

3/3,AB/9 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0219746 DBA Accession No.: 98-01343

Baculo virus expressed recombinant *pneumococcal*** *surface*** *adhesin***
-A (rPsaA) of Streptococcus pneumoniae serotype 6B- generates murine antibodies capable of passive protection in an infant mouse model of bacteremia; polyclonal, *monoclonal*** antibody generation (conference abstract)

AUTHOR: De B K; Johnson S E; Ades E W; Stinson A R; Crook J; Huebner R C; Sampson J S; Carlone G M

CORPORATE AFFILIATE: Connaught-Lab. Cent.Dis.Contr.Prev.Atlanta

CORPORATE SOURCE: Connaught Laboratories, Inc., Swiftwater, PA, USA.

JOURNAL: Abstr.Gen.Meet.Am.Soc.Microbiol. (97 Meet., 251) 1997

ISSN: 0067-2777 CODEN: 0005P

CONFERENCE PROCEEDINGS: American Society for Microbiology, 97th General Meeting, Miami Beach, FL, 4-8 May, 1997.

LANGUAGE: English

ABSTRACT: *Pneumococcal*** *surface*** *adhesin***-A (*PsaA***) from Streptococcus pneumoniae serotype 6B was expressed in Spodoptera frugiperda Sf9 and Trichoplusia ni High Five insect cell culture using the baculo virus expression system. Recombinant PsaA was partially purified by partitioning in phosphate buffered saline/Triton X-114 buffer and by D5 ionexchange filter chromatography. PsaA was expressed as an Sf9 cell-associated protein with a mol.wt. of 38,000, which partitioned in the Triton X-114 phase, and reacted with rabbit polyclonal and *monoclonal*** antibodies by dot blot and Western blot analysis. High Five cells expressed PsaA in serum-free culture medium as a cell-free soluble protein with a mol.wt. of 37,000, which did not partition in the Triton X-114 phase, and reacted with polyclonal and *monoclonal*** antibodies by ELISA and Western blot analysis. PsaA was immunogenic in Swiss-Webster adult female mice. Anti-PsaA immune serum was used for passive immunization in infant mouse bacteremic models. (0 ref)

3/3,AB/10 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2002 Thomson Derwent & ISI. All rts. reserv.

0168982 DBA Accession No.: 94-11533

The utility of recombinant protein in an enzyme immunoassay for antibodies

09/613092

against Streptococcus pneumoniae - recombinant *pneumococcal***
*surface*** *adhesin*** A antigen production, purification,
characterization and application in pneumococcal disease diagnosis
(conference abstract)

AUTHOR: Tharpe J A; Sampson J S; Stinson A R; Russel H

CORPORATE AFFILIATE: CDC

CORPORATE SOURCE: CDC, Atlanta, GA 30333, USA.

JOURNAL: Abstr.Gen.Meet.Am.Soc.Microbiol. (94 Meet., 617) 1994

CODEN: 0005P

LANGUAGE: English

ABSTRACT: Most pneumococcal diagnostic assays lack sensitivity and specificity. A 37 kDa *pneumococcal*** *surface*** *adhesin*** A (*PsaA***) shows promise as a diagnostic. To augment production, the gene encoding PsaA was cloned into expression vector plasmid pMal-CTM. The expressed protein was a maltose-binding fusion protein due to insertion of psaA downstream from the vector malE gene. The fusion protein was purified by affinity chromatography and analyzed by SDS-PAGE to determine purity and confirm migration at the expected approximate mol.wt. of 70,000. The immunoreactivity of the purified fusion protein was evaluated using polyclonal and *monoclonal*** antibody to native PsaA. The ability to utilize recombinant protein as a replacement solid-phase antigen for native protein was investigated by ELISA. Bacteremic sera from 25 patients diagnosed with pneumococcal disease were tested with both native protein and recombinant protein. Test results indicated that the fusion protein can serve as a useful substitute for native pneumococcal protein in the ELISA. (0 ref)

3/3,AB/11 (Item 4 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

(c) 2002 Thomson Derwent & ISI. All rts. reserv.

0151166 DBA Accession No.: 93-09218 PATENT

Recombinant vaccine to prevent pneumonia - comprises pneumococcal fimbrial protein-A expressed in Streptococcus pneumoniae; *monoclonal*** antibody and hybridoma

PATENT ASSIGNEE: U.S.Dept.Health-Human-Serv. 1993

PATENT NUMBER: WO 9310238 PATENT DATE: 930527 WPI ACCESSION NO.:
93-182553 (9322)

PRIORITY APPLIC. NO.: US 816286 APPLIC. DATE: 920103

NATIONAL APPLIC. NO.: WO 92US9522 APPLIC. DATE: 921116

LANGUAGE: English

ABSTRACT: A vaccine providing protection against pneumococcal pneumonia is claimed comprising pneumococcal fimbrial protein-A (PfpA) or a polypeptide derived from it in an excipient. Also claimed are: (A) a DNA sequence encoding a polypeptide corresponding to PfpA (or at least 5 contiguous amino acids of it); (B) the polypeptide of (A) free of proteins with which it is naturally associated; (C) a recombinant DNA molecule comprising a vector and the DNA of (A); (D) a cell that contains a recombinant DNA molecule as in (C); (E) an antibody (preferably a *monoclonal*** antibody (*MAB***) or binding fragment having binding affinity for PfpA; (F) a hybridoma (1E7A3D7C2) which produces the *MAB*** of (E); and (G) a diagnostic kit comprising the *MAB***. The *MAB*** was produced using pneumococcal cells as immunogen, and then used to identify cloned Streptococcus *pneumoniae*** DNA encoding the *37*** *kDa*** PfpA. PfpA was produced by expression in host cells and purified from S. pneumoniae cells. (50pp)

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3/3,AB/12 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2002 Thomson Derwent & ISI. All rts. reserv.

0111059 DBA Accession No.: 90-13750

*Monoclonal*** antibody recognizing a species-specific protein from
Streptococcus pneumoniae - potential application in disease diagnosis;
37 kDa antigen potential application in vaccine construction; hybridoma
construction

AUTHOR: Russell H; Tharpe J A; Wells D E; White E H; Johnson J E
CORPORATE SOURCE: Division of Bacterial Diseases, Center for Infectious
Diseases, Centers for Disease Control, Atlanta, Georgia 30333, USA.

JOURNAL: J.Clin.Microbiol. (28, 10, 2191-95) 1990

CODEN: JCMIDW

LANGUAGE: English

ABSTRACT: *Monoclonal*** antibodies (*Mabs***) were prepared against a
nonencapsulated strain (R36A) of Streptococcus pneumoniae in order to
isolate antigens common to this species. Female BALB/c mice were
injected 3 times i.v. and once i.p. with whole cell preparations of
strain R36A (a derivative of type 2 strain D39). Spleen cells were
fused with Sp2/0-Ag14 mouse myeloma cells to form hybridomas. Hybridoma
supernatants were tested for S. pneumoniae-specific *Mab*** production
in an ELISA. A hybridoma clone, 1E7A3D7C2, was selected. A 37 kDa
protein was identified in lysates of 24 different encapsulated strains
of S. pneumoniae using the new *Mabs*** in Western blotting. The
*Mabs*** specific for the 37 kDa antigen did not react with 55
heterologous strains representing 19 genera and 36 species of bacteria
that can also cause acute lower respiratory tract disease. Immunogold
labeling suggested that the antigen was synthesized inside the
pneumococcal cells. *Mabs*** specific for the antigen bound whole cells
in ELISA and indirect immunofluorescence assay. The 37 kDa protein may
be useful as a pneumococcus vaccine and the *Mabs*** may be useful in
disease diagnosis. (45 ref)

Set	Items	Description
S4	46	PNEUMON?(S) (37KD? OR 37KILOD? OR 37(W) (KD? OR KILOD? OR KI- LO(W) (D OR DALTON? ? OR DA)))
S5	12	S4 AND (MOAB? ? OR MAB? ? OR MONOCLON? OR 4E9 OR 1B6 OR 8G- 12 OR 6F6 OR 1E7)
S6	4	S5 NOT S2
S7	3	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 113

7/3,AB/1 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
(c) 2002 INIST/CNRS. All rts. reserv.

11009524 PASCAL No.: 93-0519031

Characterization of a heat-modifiable outer membrane protein of
Haemophilus somnus

TAGAWA Y; HARITANI M; ISHIKAWA H; YUASA N

National inst. animal health, Tsukuba, Ibaraki 305, Japan

Journal: Infection and immunity, 1993, 61 (5) 1750-1755

Language: English

In immunoblot analysis, a murine *monoclonal*** antibody (*Mab***), 27-1,
which was produced to an outer membrane protein (OMP) of Haemophilus

09/613092

sonnus, showed that a major OMP is heat modifiable, having a molecular mass of 28 kDa when the N-lauroylsarcosine-insoluble OMP preparation was solubilized at 60 °C and a mass of *37*** kDa*** when the OMP preparation was solubilized at 100 Degree C. The heat-modifiable OMP reacted intensely with convalescent sera obtained from calves with experimental H. somnus *pneumonia*** in immunoblot analysis. Immunoelectron microscopic and antibody absorption studies revealed that the *Mab*** 27-1 epitope was not surface,exposed on the intact bacterium

7/3,AB/2 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2002 European Patent Office. All rts. reserv.

01322386

Primers for synthesizing full length cDNA clones and their use
Primer zur Synthese von vollstandigen cDNA Klonen und ihre Verwendung
Amorces pour la synthese de cADN de pleine longueur et leur utilisation
PATENT ASSIGNEE:

Helix Research Institute, (2656450), 1532-3 Yana, Kisarazu-shi, Chiba
292-0812, (JP), (Applicant designated States: all)

INVENTOR:

Ota, Toshio, 1-2-7-105, Tsujido Shinmachi, Fujisawa-shi, Kanagawa
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Nishikawa, Tetsuo, 27-3-403, Hikawa-cho, Itabashi-ku, Tokyo 173-0013,
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Isogai, Takao, 511-12, Ohmuro, Ami-machi, Inashiki-gun, Ibaraki 300-0303,
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Hayashi, Koji, 1-9-446, Yushudai Nishi, Ichihara-shi, Chiba 299-0125,
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Ishii, Shizuko, 4508-19-202, Yana, Kisarazu-shi, Chiba 292-0812, (JP)
Kawai, Yuri, 4508-19-201, Yana, Kisarazu-shi, Chiba 292-0812, (JP)
Wakamatsu, Ai, 1473-4-202, Takayanagi, Kisarazu-shi, Chiba 292-0014, (JP)
Sugiyama, Tomoyasu, 2-6-23-102, Kiyomidai, Kisarazu-shi, Chiba 292-0045,
(JP)
Nagai, Keiichi, 3-44-14-9-204, Sakuragaoka, Higashiyamato-shi, Tokyo
207-0022, (JP)
Kojima, Shinichi, 2-7-10-202, Gion, Kisarazu-shi, Chiba 292-0052, (JP)
Otsuki, Tetsuji, 3-1-10-B102, Asahi, Kisarazu-shi, Chiba 292-0055, (JP)
Koga, Hisashi, 2-4-15, Asahi, Kisarazu-shi, Chiba 292-0055, (JP)

LEGAL REPRESENTATIVE:

VOSSIUS & PARTNER (100314), Siebertstrasse 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1130094 A2 010905 (Basic)
EP 1130094 A3 011121

APPLICATION (CC, No, Date): EP 2000114089 000707;

PRIORITY (CC, No, Date): JP 99194486 990708; JP 2000118774 000111; JP
2000183765 000502

DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI;
LU; MC; NL; PT; SE

EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI

INTERNATIONAL PATENT CLASS: C12N-015/12; C12N-015/11; C12N-015/10;
C12N-015/70; C12N-015/85; C12N-005/10; C12N-001/21; C07K-014/47;
C07K-016/18; C12Q-001/68

ABSTRACT EP 1130094 A2

Primers for synthesizing full length cDNAs and their use are provided.
830 cDNA encoding a human protein has been isolated and nucleotide
sequences of 5'-, and 3'-ends of the cDNA have been determined.

Searcher : Shears 308-4994

09/613092

Furthermore, primers for synthesizing the full length cDNA have been provided to clarify the function of the protein encoded by the cDNA. The full length cDNA of the present invention containing the translation start site provides information useful for analyzing the functions of the protein.

ABSTRACT WORD COUNT: 79

NOTE:

Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200136	709
SPEC A	(English)	200136	97667
Total word count - document A			98376
Total word count - document B			0
Total word count - documents A + B			98376

7/3,AB/3 (Item 2 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

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00309966

Vaccine against pasteurella

Impfstoff gegen Pasteurella

Vaccin contre pasteurella

PATENT ASSIGNEE:

BTG INTERNATIONAL LIMITED (Company No. 2664412), (1475433), 10 Fleet Place Limeburner Lane, London EC4M 7SB, (GB), (Proprietor designated states: all)

INVENTOR:

Donachie, William, 7 Beechbank Crescent, East Calder, West Lothian, EH53 0DX, (GB)

LEGAL REPRESENTATIVE:

Percy, Richard Keith et al (46441), Patents Department British Technology Group Ltd 10 Fleet Place, London EC4M 7SB, (GB)

PATENT (CC, No, Kind, Date): EP 287206 A1 881019 (Basic)
EP 287206 B1 930804
EP 287206 B2 991124

APPLICATION (CC, No, Date): EP 88301932 880304;

PRIORITY (CC, No, Date): GB 8706944 870324; GB 8721286 870910

DESIGNATED STATES: BE; DE; ES; FR; IT; NL; SE

INTERNATIONAL PATENT CLASS: A61K-039/02; C12N-001/38; C12P-021/00; C07K-001/00; C07K-001/14

ABSTRACT EP 287206 A1

A vaccine against pasteurellosis is obtained from Pasteurella grown under iron restriction conditions.

ABSTRACT WORD COUNT: 17

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9947	900
CLAIMS B	(German)	9947	934
CLAIMS B	(French)	9947	1005
SPEC B	(English)	9947	6261

Searcher : Shears 308-4994

09/613092

Total word count - document A 0
Total word count - document B 9100
Total word count - documents A + B 9100

Set	Items	Description
S8	349	AU=(ADES, E? OR ADES E?)
S9	10042	AU=(JOHNSON, S? OR JOHNSON S?)
S10	174	AU=(JUE, D? OR JUE D?)
S11	873	AU=(SAMPSON, J? OR SAMPSON J?)
S12	265	AU=(CARLONE, G? OR CARLONE G?)
S13	7	S8 AND S9 AND S10 AND S11 AND S12
S14	51	S8 AND (S9 OR S10 OR S11 OR S12)
S15	29	S9 AND (S10 OR S11 OR S12)
S16	10	S10 AND (S11 OR S12)
S17	55	S11 AND S12
S18	48	(S14 OR S15 OR S17 OR S8 OR S9 OR S10 OR S11 OR S12) AND (-

- Author (S)

~~S19 1103409 (S13 OR S16 OR S18) NOT (S2 OR S6)~~
S20 39 (S13 OR S16 OR S18) NOT (S2 OR S6)
S21 21 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

21/3,AB/1 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
(c) 2002 BLDSC all rts. reserv. All rts. reserv.

02433820 INSIDE CONFERENCE ITEM ID: CN025429609
Intranasal Immunization with Recombinant PsaA (*37kDa"**) Protects Mice
Challenged Intranasally with Streptococcus *pneumoniae"***
*Ades, E. W."**"; *Sampson, J. S."**"; Ebriles, D. E.; King, J. D.
CONFERENCE: Emerging infectious diseases-International conference
P: P-1.8
(np), 1998
LANGUAGE: English DOCUMENT TYPE: Conference Abstracts and programme
CONFERENCE SPONSOR: Centers for Disease Control and Prevention
Council of State and Territorial Epidemiologists
American Society for Microbiology
CONFERENCE LOCATION: Atlanta, GA
CONFERENCE DATE: Mar 1998 (199803) (199803)
NOTE:
See also 5138.540 vol 48 no 3 1998 for report

21/3,AB/2 (Item 1 from file: 77)
DIALOG(R)File 77:Conference Papers Index
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4371412
Supplier Accession Number: 98-04409 V26N04
Mapping and immunogenicity of phage display library selected peptides of
the pneumococcal PsaA common protein
Zeiler, J.; Sampson, J.S.; Carlone, G.M.; Ades, E.W.; Tharpe, J.A.;
Westerink, M.A.J.
Med. Coll. OH, Toledo, OH, USA
International Conference on Emerging Infectious Diseases 9815009
Atlanta, GA (USA) 8-11 Mar 1998
Centers for Disease Control and Prevention, Council of State and
Territorial Epidemiologists, American Society for Microbiology, National

09/613092

Foundation for CDC

Centers for Disease Control and Prevention, 1600 Clifton Road, NE,
Atlanta, GA 30333, USA; phone: (404) 639-3311; URL: <http://www.cdc.gov>,
Abstracts available.

21/3,AB/3 (Item 2 from file: 77)
DIALOG(R)File 77:Conference Papers Index
(c) 2002 Cambridge Sci Abs. All rts. reserv.

4371410

Supplier Accession Number: 98-04409

V26N04

Possible relationship of pneumococcal surface adhesin A antibody level to
nasopharyngeal carriage of Streptococcus pneumoniae in young African
infants

Obaro, S.K.; McAdam, K.J.W.P.; Tharpe, J.A.; Ades, E.; Carlone, G.M.;
Sampson, J.S.

MRC Labs., Gambia, Africa

International Conference on Emerging Infectious Diseases 9815009
Atlanta, GA (USA) 8-11 Mar 1998

Centers for Disease Control and Prevention, Council of State and
Territorial Epidemiologists, American Society for Microbiology, National
Foundation for CDC

Centers for Disease Control and Prevention, 1600 Clifton Road, NE,
Atlanta, GA 30333, USA; phone: (404) 639-3311; URL: <http://www.cdc.gov>,
Abstracts available.

21/3,AB/4 (Item 3 from file: 77)
DIALOG(R)File 77:Conference Papers Index
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02852407

Supplier Accession Number: 92002407

V20N01

Molecular cloning of the gene encoding the 37-kDa protein of
Streptococcus pneumoniae

Sampson, J.; O'Connor, S.; Stinson, A.; Tharpe, J.; Russell, H.

CDC, Atlanta, GA

91st General Meeting of the American Society for Microbiology 9120375
Dallas, TX (USA) 5-9 May 1991

American Society for Microbiology

ASM, 1325 Massachusetts Avenue NW, Washington, DC 20005, USA, Poster
Paper No. D112

21/3,AB/5 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
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15105958 PASCAL No.: 01-0266360

Natural development of antibodies to pneumococcal surface protein A,
*pneumococcal*** *surface*** *adhesin*** A, and pneumolysin in relation to
pneumococcal carriage and acute otitis media

RAPOLA Satu; JAENTTI Virva; HAIKALA Raili; SYRJAENEN Ritva; *CARLONE
George M***; *SAMPSON Jacquelyn S***; BRILES David E; PATON James C; TAKALA
Aino K; KILPI Terhi M; KAEYHTY Helena

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09/613092

Alabama, Birmingham, United States; Women's and Children's Hospital,
Adelaide, Australia

Journal: The Journal of infectious diseases, 2000, 182 (4) 1146-1152

Language: English

*Pneumococcal*** surface protein A (PspA), *pneumococcal*** *surface***
*adhesin*** A (*PsaA***), and pneumolysin (Ply) are common to virtually all
Streptococcus pneumoniae isolates. They are immunogenic and protective
against pneumococcal challenge in animals and are the major candidates for
a protein-based pneumococcal vaccine for humans. However, little is known
of the natural development of antibodies to these proteins in humans. The
objective of this study was to evaluate the natural development of
antibodies to PspA, *PsaA***, and Ply in relation to *pneumococcal***
infection and carriage in young children. Serum antibodies to these
proteins were measured by EIA in children at ages 6, 12, 18, and 24 months
and in their mothers. All age groups were capable of producing antibodies
to the 3 proteins. The antibody concentrations increased with age and were
strongly associated with pneumococcal exposure, whether by carriage or
infection (acute otitis media).

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21/3,AB/6 (Item 2 from file: 144)

DIALOG(R)File 144:Pascal

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14900580 PASCAL No.: 01-0049034

Streptococcus pneumoniae serotype 4 outbreak in A home for the aged :
Report and review of recent outbreaks

GLEICH Sheldon; MORAD Yosef; ECHAGUE Ramon; MILLER James R; KORNBLUM John
; *SAMPSON Jacquelyn S***; BUTLER Jay C

Division of Infectious Diseases, St John's Episcopal Hospital, Far
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New York, United States; Molecular Typing Laboratory, New York City
Department of Health, New York, New York, United States; Respiratory
Diseases Branch, National Center for Infectious Diseases, Centers for
Disease Control and Prevention, Atlanta, Georgia, United States

Journal: Infection control and hospital epidemiology, 2000, 21 (11)
711-717

Language: English

OBJECTIVE: To describe a *pneumonia*** outbreak caused by Streptococcus
*pneumoniae*** among residents of a home for the aged and to review
contemporary pneumococcal outbreaks. DESIGN: Epidemiological investigation.
METHODS: S *pneumoniae*** isolates were serotyped and analyzed by
pulsed-field gel electrophoresis. Paired sera were tested for antibodies to
*pneumococcal*** *surface*** *adhesin*** A protein (*PsaA***, a *37***-
*kDa*** cell-wall protein). *Pneumococcal*** outbreaks reported in the last
decade in English were reviewed. RESULTS: *Pneumonia*** developed in 18 of
200 residents. In 11 (61%), a pneumococcal etiology was demonstrated. S
*pneumoniae***, serotype 4, was isolated from the blood cultures of 3
patients; all isolates were indistinguishable by pulsed-field gel
electrophoresis. Pneumococcal involvement was established in 2 by sputum
culture and latex agglutination of parapneumonic fluid and in 6 others by a
twofold rise in optical density of serum antibody reactive to *PsaA***.
*Pneumococcal*** immunization had not previously been received by any
patient; mortality was 22%. No additional cases were noted following

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administration of pneumococcal vaccine and antibiotic prophylaxis with penicillin or erythromycin. Twenty-six outbreaks of invasive pneumococcal disease since 1990 were reviewed. Twelve occurred in the United States, and serotypes 23F, 14, and 4 accounted for 8 (67%) of 12 outbreaks. All confirmed serotypes in US outbreaks are included in the 23-valent vaccine. More than one half of pneumococcal outbreaks worldwide involved elderly persons in hospitals or long-term-care facilities. CONCLUSIONS: A pneumococcal *pneumonia*** outbreak occurred among unvaccinated residents of a residential facility for the aged. Institutionalized elderly persons are at risk of outbreaks of pneumococcal disease and should be vaccinated.

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21/3,AB/7 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal
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14896854 PASCAL No.: 01-0045066

*Pneumococcal*** *surface*** *adhesin*** A antibody concentration in serum and nasopharyngeal carriage of Streptococcus pneumoniae in young African infants

OBARO S K; ADEGBOLA R A; THARPE J A; *ADES E W***; MCADAM K P W J;
*CARLONE G***; *SAMPSON J S***

MRC Laboratories, PO Box 273, Fajara, Banjul, Gambia; CDC, Atlanta, GA, United States

Journal: Vaccine, 2000, 19 (4-5) 411-412

Language: English

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21/3,AB/8 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal
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14665225 PASCAL No.: 00-0338354

Purification and characterization of Streptococcus pneumoniae palmitoylated *pneumococcal*** *surface*** *adhesin*** A expressed in Escherichia coli

DE B K; *SAMPSON J S***; *ADES E W***; HUEBNER R C; *JUE D L***; *JOHNSON S E***; ESPINA M; STINSON A R; BRILES D E; *CARLONE G M***

Division of Bacterial and Mycotic Diseases, and Biotechnology Core Facility Branch, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, United States; Pasteur Merieux Connaught Laboratories, Inc, Swiftwater, PA 18370, United States; Department of Microbiology, University of Alabama, Birmingham, AL 35294, United States

Journal: Vaccine, 2000, 18 (17) 1811-1821

Language: English

All Streptococcus pneumoniae isolates tested to date express a species-common lipoprotein designated as *pneumococcal*** *surface*** *adhesin*** A (*PsaA***). This protein is cell-associated, hydrophobic, immunogenic, and genetically conserved. It is currently under investigation as a potential component in third-generation pneumococcal vaccine formulations. To overcome the problem of low-level expression of native hydrophobic PsaA in S. pneumoniae, and also of the recombinant PsaA (rPsaA) in Escherichia coli, we generated a stable E. coli construct expressing functional palmitoylated rPsaA (similar 10 mg/l of fermentation culture)

using *Borrelia burgdorferi* outer surface protein A (OspA, a hydrophobic lipoprotein) signal peptide. By Western blot analysis, the chimeric rPsaA (similar 34 kDa) was detected in the cell lysate using anti-PsaA antibodies. It was partially purified by extracting the cell pellet with PBS/Triton X SUP R -114 buffers, followed by anion exchange filter chromatography. A trypsin digestion profile of rPsaA closely resembled that of the native protein, as revealed by SDS-PAGE/silver staining. Lipidation of rPsaA was confirmed by labeling recombinant *E. coli* cells with (SUP 3 H) palmitic acid and analyzing the labeled *E. coli* cells by Western blotting coupled with autoradiography. Further, analysis of purified rPsaA by mass spectrometry (MALDI-TOF) revealed a heterogenous spectrum with a major peak (M+H) SUP + SUP 1 of mass 33,384 Da (theoretical mass of palmitoylated rPsaA=33,361 Da). Purified rPsaA was immunogenic in CBA/NCAHN-XID female mice following intranasal immunization with or without adjuvant, as determined by measurement of anti-PsaA serum IgG levels. These anti-PsaA antibodies reacted with both native and rPsaA polypeptides. Our data strongly suggest that *E. coli*-expressed rPsaA is palmitoylated and closely resembles the native protein in structure and immunogenicity. It was also observed to elicit measurable protection against nasopharyngeal carriage with *S. pneumoniae*.

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21/3,AB/9 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal
(c) 2002 INIST/CNRS. All rts. reserv.

14502824 PASCAL No.: 00-0166015

Confirmation of psaA in all 90 serotypes of *Streptococcus pneumoniae* by PCR and potential of this assay for identification and diagnosis

MORRISON K E; LAKE D; CROOK J; *CARLONE G M***; *ADES E***; FACKLAM R; *SAMPSON J S***

Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, Atlanta, Georgia 30333, United States

Journal: Journal of clinical microbiology, 2000, 38 (1) 434-437

Language: English

The gene encoding the *pneumococcal*** *surface*** *adhesin*** A (*PsaA***) protein, *psaA***, was confirmed in all *Streptococcus pneumoniae* serotypes by a newly developed PCR (psaA PCR) assay. Eighty-nine of the 90 serotypes amplified produced an 838-bp fragment; the exception was a serotype 16F strain acquired from the American Type Culture Collection (ATCC). Analysis of 20 additional 16F strains from the United States and Brazil showed that the gene was amplified in all 16F strains, implying that the serotype 16F ATCC strain must be a variant. The specificity of the assay was verified by the lack of signal from analysis of heterologous bacterial species (n = 30) and genera (n = 14), including viridans group streptococci. The potential of the assay for clinical application was shown by its ability to detect *pneumococci*** in culture-positive nasopharyngeal specimens. Demonstration of *psaA*** in all 90 serotypes and lack of amplification of heterologous organisms suggest that this assay could be a useful tool for detection of pneumococci and diagnosis of disease.

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21/3,AB/10 (Item 6 from file: 144)

DIALOG(R)File 144:Pascal
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14447865 PASCAL No.: 00-0106623

Intranasal immunization of mice with a mixture of the *pneumococcal*** proteins *PsaA*** and PspA is highly protective against nasopharyngeal carriage of Streptococcus pneumoniae

BRILES D E; *ADES E***; PATON J C; *SAMPSON J S***; *CARLONE G M***; HUEBNER R C; VIROLAINEN A; SWIATLO E; HOLLINGSHEAD S K

Department of Microbiology, University of Alabama at Birmingham, Birmingham, Alabama, United States; Department of Pediatrics, University of Alabama at Birmingham, Birmingham, Alabama, United States; Centers for Disease Control and Prevention, Atlanta, Georgia, United States; Molecular Microbiology Unit, Women's and Children's Hospital, North Adelaide, Australia; Pasteur Merieux Connaught, Swiftwater, Pennsylvania, United States; Haartman Institute, Department of Bacteriology and Immunology, University of Helsinki, Finland; Division of Infectious Diseases, University of Mississippi Medical Center, Jackson, Mississippi, United States

Journal: Infection and immunity, 2000, 68 (2) 796-800

Language: English

Acquisition of pneumococci is generally from carriers rather than from infected individuals. Therefore, to induce herd immunity against Streptococcus pneumoniae it will be necessary to elicit protection against carriage. Capsular polysaccharide-protein conjugates, PspA, and *PsaA*** are known to elicit some protection against nasopharyngeal carriage of *pneumococci*** but do not always completely eliminate carriage. In this study, we observed that PsaA elicited better protection than did PspA against carriage. Pneumolysin elicited no protection against carriage. Immunization with a mixture of PsaA and PspA elicited the best protection against carriage. These results indicate that PspA and PsaA may be useful for the elicitation of herd immunity in humans. As PspA and pneumolysin are known to elicit immunity to bacteremia and pneumonia, their inclusion in a mucosal vaccine may enable such a vaccine to prevent invasive disease as well as carriage.

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21/3,AB/11 (Item 7 from file: 144)
DIALOG(R)File 144:Pascal
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12993874 PASCAL No.: 97-0273786

Limited diversity of streptococcus pneumoniae *psaA*** among *pneumococcal*** vaccine serotypes

*SAMPSON J S***; FURLOW Z; WHITNEY A M; WILLIAMS D; FACKLAM R; *CARLONE G M***

Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, United States

Journal: Infection and immunity, 1997, 65 (5) 1967-1971

Language: English

The *pneumococcal*** *surface*** *adhesin*** A (*PsaA***) is a surface-exposed protein of the gram-positive bacterium Streptococcus pneumoniae. It belongs to a group of proteins designated the lipoprotein receptor I antigen family. The gene encoding *PsaA*** from an encapsulated strain of *pneumococcal*** serotype 6B was cloned and sequenced. The

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peptide sequence was compared to that of homologs found in *S. pneumoniae* serotype 2, *viridans streptococci*, and *Enterococcus faecalis*. Identity values among the deduced peptides ranged from 57 to 98%. The polymorphism of *psaA* was examined among the 23 encapsulated vaccine serotypes by using PCR-restriction fragment length polymorphism analysis. Ten different enzymes were used to analyze 80 strains representing the 23 serotypes in a 23-valent polysaccharide vaccine. This analysis showed that restriction sites within the gene were highly conserved, with only a minor variation occurring in 10% of the strains, the result of an additional Tsp509I site. The lack of variation for the other restriction sites within the gene examined here indicates that *psaA* is genetically conserved, an important characteristic necessary for a candidate common protein vaccine.

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21/3,AB/12 (Item 8 from file: 144)
DIALOG(R)File 144:Pascal
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11380897 PASCAL No.: 94-0208013

Cloning and nucleotide sequence analysis of *psaA*, the *Streptococcus pneumoniae**** gene encoding a *37***-kilodalton*** protein homologous to previously reported *Streptococcus sp. adhesins*

*SAMPSON J S***; O'CONNOR S P; STINSON A R; THARPE J A; RUSSELL H

Cent. disease control prevention, national cent. infectious diseases,
div. bacterial mycotic disease, Atlanta GA 30333, USA

Journal: Infection and immunity, 1994, 62 (1) 319-324

Language: English

Gene *psaA*, which encodes the *Streptococcus pneumoniae* 37-kDa protein, was cloned in *Escherichia coli*, and its complete nucleotide sequence was determined. Analysis of the sequence of the 2.4-kb cloned fragment revealed three open reading frames (ORFs). ORF2, which is 933 bp long, was identified as *psaA*. The two other ORFs identified flank *psaA*. ORF1, located upstream of *psaA*, is 836 nucleotides long and encodes a protein with a calculated molecular mass of 29,843 Da. The sequence for ORF3, located downstream of *psaA*, was only partially determined. Northern (RNA) blot analysis of pneumococcal RNA suggests that *psaA* is transcribed as part of a polycistronic message

21/3,AB/13 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2002 Inst for Sci Info. All rts. reserv.

13586721 Document Delivery Available: 000174457600039 References: 52

TITLE: Newly characterized species-specific immunogenic *Chlamydomonas pneumoniae* peptide reactive with murine monoclonal and human serum antibodies

AUTHOR(S): Marston EL (REPRINT); James AV; Parker JT; Hart JC; Brown TM; Messmer TO; *Jue DL***; Black CM; *Carlone GM***; Ades EW; *Sampson J***
AUTHOR(S) E-MAIL: EMARSTON@CDC.GOV

CORPORATE SOURCE: CDCP, Natl Ctr Infect Dis, US Dept Hlth & Human Serv, /Atlanta//GA/30333 (REPRINT); CDCP, Natl Ctr Infect Dis, US Dept Hlth & Human Serv, /Atlanta//GA/30333; CDCP, US Dept HHS, /Atlanta//GA/30333

PUBLICATION TYPE: JOURNAL

PUBLICATION: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, 2002, V9, N2 (MAR), P446-452

Searcher : Shears 308-4994

09/613092

GENUINE ARTICLE#: 532EA

PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904
USA

ISSN: 1071-412X

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: A monoclonal antibody (MAB) directed against an unknown *Chlamydophila pneumoniae* epitope has been characterized, and the respective peptide mimotope has been identified. A murine MAB specific for *C. pneumoniae* was used to select peptides from phage display libraries. The peptides identified from the phage display library clones reacted specifically with the respective target murine MAB and with human sera previously identified as having antibody titers to *C. pneumoniae*. The selected peptide mimotope sequences tended to be composed of charged residues surrounding a core of hydrophobic residues. The peptide with the best binding could inhibit >95% of binding to the MAB, suggesting that the selected peptide binds the paratope of the respective MAB. The peptide reacted with human sera previously determined by microimmunofluorescence to have anti-*C. pneumoniae* antibodies. The peptide was competitively competed with the MAB against Renografin-purified, sonicated *C. pneumoniae* in an enzyme-linked immunosorbent assay and with whole-cell *C. pneumoniae* in an indirect fluorescence assay format, demonstrating its potential utility in the development of diagnostics. The use of this novel peptide may allow investigators to establish standardized assays free from cross-reactive *Chlamydia trachomatis* and *Chlamydophila psittaci* epitopes and immunoreactivity.

21/3,AB/14 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2002 Inst for Sci Info. All rts. reserv.

11454942 References: 40

TITLE: Purification and characterization of *Streptococcus pneumoniae* palmitoylated *pneumococcal*** *surface*** *adhesin*** A expressed in *Escherichia coli*

AUTHOR(S): De BK (REPRINT); *Sampson JS***; *Ades EW***; Huebner RC; *Jue DL***; *Johnson SE***; Espina M; Stinson AR; Briles DE; *Carlone GM***

AUTHOR(S) E-MAIL: bkd1@cdc.gov

CORPORATE SOURCE: Ctr Dis Control & Prevent, Div Bacterial & Mycot Dis, MS G05, 1600 Clifton Rd NE/Atlanta//GA/30333 (REPRINT); Ctr Dis Control & Prevent, Div Bacterial & Mycot Dis, /Atlanta//GA/30333; Ctr Dis Control & Prevent, Natl Ctr Infect Dis, /Atlanta//GA/30333; Pasteur Merieux Connaught Labs Inc, /Swiftwater//PA/18370; Univ Alabama, Dept Microbiol, /Birmingham//AL/35294

PUBLICATION TYPE: JOURNAL

PUBLICATION: VACCINE, 2000, V18, N17 (MAR 6), P1811-1821

GENUINE ARTICLE#: 294EN

PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND

ISSN: 0264-410X

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: All *Streptococcus pneumoniae* isolates tested to date express a species-common lipoprotein designated as *pneumococcal*** *surface*** *adhesin*** A (*PsaA***). This protein is cell-associated, hydrophobic, immunogenic, and genetically conserved. It is currently under investigation as a potential component in third-generation pneumococcal vaccine formulations. To overcome the problem of low-level expression of native

hydrophobic PsaA in *S. pneumoniae*, and also of the recombinant PsaA (rPsaA) in *Escherichia coli*, we generated a stable *E. coli* construct expressing functional palmitoylated rPsaA (similar to 10 mg/l of fermentation culture) using *Borrelia burgdorferi* outer surface protein A (OspA, a hydrophobic lipoprotein) signal peptide. By Western blot analysis, the chimeric rPsaA (similar to 34 kDa) was detected in the cell lysate using anti-PsaA antibodies. It was partially purified by extracting the cell pellet with PBS/Triton X-R-114 buffers, followed by anion exchange filter chromatography. A trypsin digestion profile of rPsaA closely resembled that of the native protein, as revealed by SDS-PAGE/silver staining. Lipidation of rPsaA was confirmed by labeling recombinant *E. coli* cells with [H-3] palmitic acid and analyzing the labeled *E. coli* cells by Western blotting coupled with autoradiography. Further, analysis of purified rPsaA by mass spectrometry (MALDI-TOF) revealed a heterogenous spectrum with a major peak (M + H)(+1) of mass 33,384 Da (theoretical mass of palmitoylated rPsaA = 33,361 Da). Purified rPsaA was immunogenic in CBA/NCAHN-XID female mice following intranasal immunization with or without adjuvant, as determined by measurement of anti-PsaA serum IgG levels. These anti-PsaA antibodies reacted with both native and rPsaA polypeptides. Our data strongly suggest that *E. coli*-expressed rPsaA is palmitoylated and closely resembles the native protein in structure and immunogenicity. It was also observed to elicit measurable protection against nasopharyngeal carriage with *S. pneumoniae*. Published by Elsevier Science Ltd.

21/3,AB/15 (Item 3 from file: 440)
 DIALOG(R)File 440:Current Contents Search(R)
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09528099 References: 30

TITLE: Comparison of a *pneumococcal*** common protein (*PsaA***) antibody ELISA and a *PsaA*** immune complex ELISA for detection of *pneumococcal*** serum antibody
 AUTHOR(S): Tharpe JA; Russell H; Leinonen M; Plikaytis BD; Breiman RF; *Carlone GM***; *Ades EW***; *Sampson JS (REPRINT)***
 CORPORATE SOURCE: CTR DIS CONTROL & PREVENT,NATL CTR INFECT DIS, DIV BACTERIAL & MYCOT DIS, RESP DIS BRANCH, MS G05/ATLANTA//GA/30333 (REPRINT); CTR DIS CONTROL & PREVENT,NATL CTR INFECT DIS, DIV BACTERIAL & MYCOT DIS, RESP DIS BRANCH/ATLANTA//GA/30333; CTR DIS CONTROL & PREVENT,NATL CTR INFECT DIS, DIV BACTERIAL & MYCOT DIS/ATLANTA//GA/30333; NATL PUBL HLTH INST,/HELSINKI//FINLAND/
 PUBLICATION TYPE: JOURNAL
 PUBLICATION: PATHOBIOLOGY, 1998, V66, N2 (MAR-APR), P77-83
 GENUINE ARTICLE#: ZR445
 PUBLISHER: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND
 ISSN: 1015-2008
 LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: We examined and compared results from three assays, an enzyme-linked immunosorbent assay (ELISA) and two immune complex ELISAs for analysis of the serum antibody response to a native pneumococcal *37***- *kD*** common cell-wall protein by using acute-and convalescent-phase sera from 56 patients with community-acquired *pneumonia***. The sensitivities of the ELISA, the undissociated and dissociated immune complex assays were 85% (23 of 27), 78% (21 of 27) and 67% (18 of 27), respectively. To determine specificity, paired sera from patients with *pneumonia*** of other bacterial etiologies were tested. The specificities were 83, 83 and 72% for the ELISA, undissociated immune complex, and dissociated immune

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complex, respectively. Based on this study, the sensitivities of the three assays were not statistically different. These tests could be used retrospectively to confirm invasive pneumococcal disease.

21/3,AB/16 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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01404346
MULTIPLE ANTIGENIC PEPTIDES IMMUNOGENIC AGAINST i STREPTOCOCCUS PNEUMONIAE
/i
PEPTIDES A ANTIGENES MULTIPLES ASSURANT L'IMMUNITE CONTRE i STREPTOCOCCUS
PNEUMONIAE /i
PATENT ASSIGNEE:

The Government of the United States of America, as represented by the
Secretary, Department of Health & Human Services, (3095392), Technology
Transfer Office, Centers for Disease Control and Prevention, 1600
Clifton Road, N.E., MS E-67, Atlanta, Georgia 30333, (US), (Applicant
designated States: all)

INVENTOR:

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*JUE, Danny, L."**, 6725 Hampshire Drive, N.W., Tucker, GA 30084, (US)
*SAMPSON, Jacquelyn, S."**, 4220 Greentree Lane, College Park, GA 30349,
(US)

*CARLONE, George, M."**, 5243 Sandy Lane, Stone Mountain, GA 30087, (US)

PATENT (CC, No, Kind, Date):

WO 200204497 020117

APPLICATION (CC, No, Date): EP 2001950993 010710; WO 2001US21626 010710

PRIORITY (CC, No, Date): US 613092 000710

DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI;
LU; MC; NL; PT; SE; TR

EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI

INTERNATIONAL PATENT CLASS: C07K-014/315

LANGUAGE (Publication,Procedural,Application): English; English; English

21/3,AB/17 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
(c) 2002 Thomson Derwent & ISI. All rts. reserv.

0270256 DBA Accession No.: 2001-10010 PATENT

New *37*** *kDa*** pneumococcal surface adhesion-A protein from
Streptococcus *pneumoniae***, useful as a vaccine for treating or
preventing infections caused by Streptococcus *pneumoniae*** -
recombinant protein gene production useful in gene therapy

AUTHOR: *Sampson J S***; Russell H; Tharpe J A; *Ades E W***; *Carlone
G M***

CORPORATE SOURCE: Washington, DC, USA.

PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 2001

PATENT NUMBER: US 6217884 PATENT DATE: 20010417 WPI ACCESSION NO.:

2001-289821 (2030)

PRIORITY APPLIC. NO.: US 221753 APPLIC. DATE: 19981228

NATIONAL APPLIC. NO.: US 221753 APPLIC. DATE: 19981228

LANGUAGE: English

ABSTRACT: An isolated and purified Streptococcus pneumoniae 37,000 surface
adhesion-A protein (I) encoded by a 1,330 bp sequence (II), fully

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defined is claimed. Also claimed are: a vaccine containing (I) and a carrier; and providing a protective immune response against Streptococcus pneumoniae infection in a subject, by administering the vaccine. (I) is useful as a vaccine component as well as a reagent for identifying host antibodies raised against S. pneumoniae during infection. (I) may also be used to detect the presence of S. pneumoniae. The protein or the nucleic acid encoding it is useful for treating or preventing S. pneumoniae infection. The nucleic acids can be used as DNA primers for amplifying nucleic acids from other strains of S. pneumoniae to isolate allelic variants of the protein or for reverse transcription techniques of protein RNA, and as DNA probes for use in detection techniques such as DNA hybridization. (20pp)

21/3,AB/18 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0265207 DBA Accession No.: 2001-04961 PATENT
Immunological composition for inducing an immunological response in an animal comprises pneumococcal proteins or vector encoding the proteins - recombinant vaccine
AUTHOR: Huebner R C; *Sampson J S***; *Carlone G M***; *Ades E***; Briles D E
CORPORATE SOURCE: Birmingham, AL, USA; Swiftwater, PA, USA; Atlanta, GA, USA.
PATENT ASSIGNEE: Univ.Alabama-Res.Found.; Aventis; U.S.Cent.Dis.Contr.Prev.Atlanta 2000
PATENT NUMBER: WO 200076541 PATENT DATE: 20001221 WPI ACCESSION NO.: 2001-091328 (2010)
PRIORITY APPLIC. NO.: US 587833 APPLIC. DATE: 20000606
NATIONAL APPLIC. NO.: WO 2000US40176 APPLIC. DATE: 20000609
LANGUAGE: English
ABSTRACT: An immunological combination composition (I) is claimed. (I) contains a *pneumococcal*** *surface*** *adhesion*** protein-A (*PsaA***), an epitope of it or a vector that expresses *PsaA*** or the epitope, and *pneumococcal*** surface *PsaA*** or C or epitope of them or vectors that express them or their epitopes, or containing a vector that expresses two PsaA or epitopes of them, or PspC or an epitope of it. (I) further contains adjuvant, e.g. cholera toxin subunit-B or alum. Also claimed are: inducing an immunological response in an animal; immunizing a host against pneumococcal infection; an immunogenic composition for intranasal administration to a host susceptible to pneumococcal carriage to elicit a protective immunological response against colonization with Staphylococcus pneumoniae in the nasopharynx. The composition is used as a vaccine to induce an immunological response in an animal or immunize a host against pneumococcal infection. (38pp)

21/3,AB/19 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0250323 DBA Accession No.: 2000-04813
Purification and characterization of Streptococcus pneumoniae palmitoylated *pneumococcal*** *surface*** *adhesion*** A expressed in Escherichia coli - with the construction of a stable construct

09/613092

AUTHOR: De B K; *Sampson J S***; *Ades E W***; Huebner R C; *Jue D L***
; *Johnson S E***; Espina M; Stinson A R; Briles D E; Carlone G M

CORPORATE AFFILIATE: Nat.Cent.Infec.Dis.Atlanta
Pasteur-Merieux-Connaught-Lab. Univ.Alabama

CORPORATE SOURCE: Division of Bacterial and Mycotic Diseases, and
Biotechnology Core Facility Branch, National Center for Infectious
Diseases, Centers for Disease Control and Prevention, Atlanta, GA
30333, USA. email:bkdl@cdc.gov

JOURNAL: Vaccine (18, 17, 1811-21) 2000

ISSN: 0264-410X CODEN: VACCDE

LANGUAGE: English

ABSTRACT: All Streptococcus pneumoniae isolates tested to date express a
species-common lipoprotein designated as *pneumococcal*** *surface***
*adhesion***-A (*PsaA***). This protein is cell-associated,
hydrophobic, immunogenic, and genetically conserved. To overcome the
problem of low-level expression of native hydrophobic PsaA in S.
pneumoniae, and also of the recombinant PsaA (rPsaA) in Escherichia
coli, a stable E. coli construct was generated expressing functional
palmitoylated rPsaA using Borrelia burgdorferi outer surface protein A
signal peptide. By Western blot hybridization, the chimeric rPsaA was
detected in the cell lysate using anti-PsaA antibodies. It was
partially purified by extracting the cell pellet with PBS/Triton XR-114
buffers, followed by anion-exchange filter chromatography. A trypsin
(EC-3.4.21.4) digestion profile of rPsaA closely resembled that of the
native protein, as revealed by SDS-PAGE/silver staining. E. coli
expressed rPsaA was palmitoylated and closely resembled the native
protein in structure and immunogenicity. It also elicited measurable
protection against nasopharyngeal carriage with S. pneumoniae. (40 ref)

21/3,AB/20 (Item 4 from file: 357)

DIALOG(R)File 357:Derwent Biotech Res.

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0243064 DBA Accession No.: 1999-13829 PATENT

Recombinant lipidated pneumococcal surface protein-A useful for
immunization of animals against pneumococcal infection - plasmid
pOPsaA.1-mediated gene transfer and expression in Escherichia coli,
used for Streptococcus pneumoniae infection recombinant vaccine

AUTHOR: *Ades E W***; *Carlone G M***; De D K; *Sampson J S***; Huebner
R C

CORPORATE SOURCE: Atlanta, GA, USA.

PATENT ASSIGNEE: U.S.Cent.Dis.Contr.Prev.Atlanta 1999

PATENT NUMBER: WO 9940200 PATENT DATE: 19990812 WPI ACCESSION NO.:
1999-508505 (1942)

PRIORITY APPLIC. NO.: US 17782 APPLIC. DATE: 19980203

NATIONAL APPLIC. NO.: WO 99US379 APPLIC. DATE: 19990114

LANGUAGE: English

ABSTRACT: A hybrid polynucleotide containing a first sequence encoding a
signal peptide of lipoprotein other than the *pneumococcal*** surface
protein-A (*PsaA***) and contiguous with a second sequence encoding a
mature PsaA protein (37,000 D), is new. Also claimed are: an expression
vector (e.g. plasmid pOPsaA.1); preparation of the recombinant
lipidated PsaA protein, where following the protein expression the host
cells (e.g. Escherichia coli) are lysed with a surfactant and separated
using a chromatographic column to release the recombinant PsaA protein;
the recombinant PsaA protein; and an immunological composition
containing the recombinant PsaA protein. The immunological composition

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containing the PsaA protein forms a method of inducing an immunological response in an animal. The composition is also used to immunize a host against pneumococcal infection, especially Streptococcus pneumoniae. (40pp)

21/3,AB/21 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0233199 DBA Accession No.: 99-03300 PATENT
Nucleic acid encoding the *37*** *kDa*** surface adhesin-A of Streptococcus *pneumoniae*** - vector-mediated gene transfer and expression in host cell, antibody, DNA probe and DNA primer, used for infection diagnosis, therapy, recombinant vaccine or nucleic acid vaccine
AUTHOR: *Sampson J S***; Russell H; Tharpe J A; *Ades E W***; *Carlone G M***

CORPORATE SOURCE: Washington, DC, USA.

PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 1998

PATENT NUMBER: US 5854416 PATENT DATE: 981229 WPI ACCESSION NO.:

99-095007 (9908)

PRIORITY APPLIC. NO.: US 715131 APPLIC. DATE: 960917

NATIONAL APPLIC. NO.: US 715131 APPLIC. DATE: 960917

LANGUAGE: English

ABSTRACT: A new and specified DNA sequence encodes the surface adhesin-A of Streptococcus pneumoniae with a mol.wt. value of 37,000 and a specified 390 amino acid protein sequence. Also claimed are fragments of the new DNA consisting of at least 50 nucleotides, specified oligonucleotides, and vectors containing the DNA. The DNA may be used to produce a recombinant protein, as a source of DNA probes and DNA primers for isolation of related sequences and for infection diagnosis, in nucleic acid vaccines or to prepare recombinant vaccines, and to raise antibodies for use in infection therapy. The N- and C-terminal coding regions of the gene for serotype-6B are used as DNA primers for polymerase chain reaction-restriction fragment length polymorphism analysis as they can amplify the adhesin-A gene from all 23 of the vaccinating serotypes. (19pp)

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